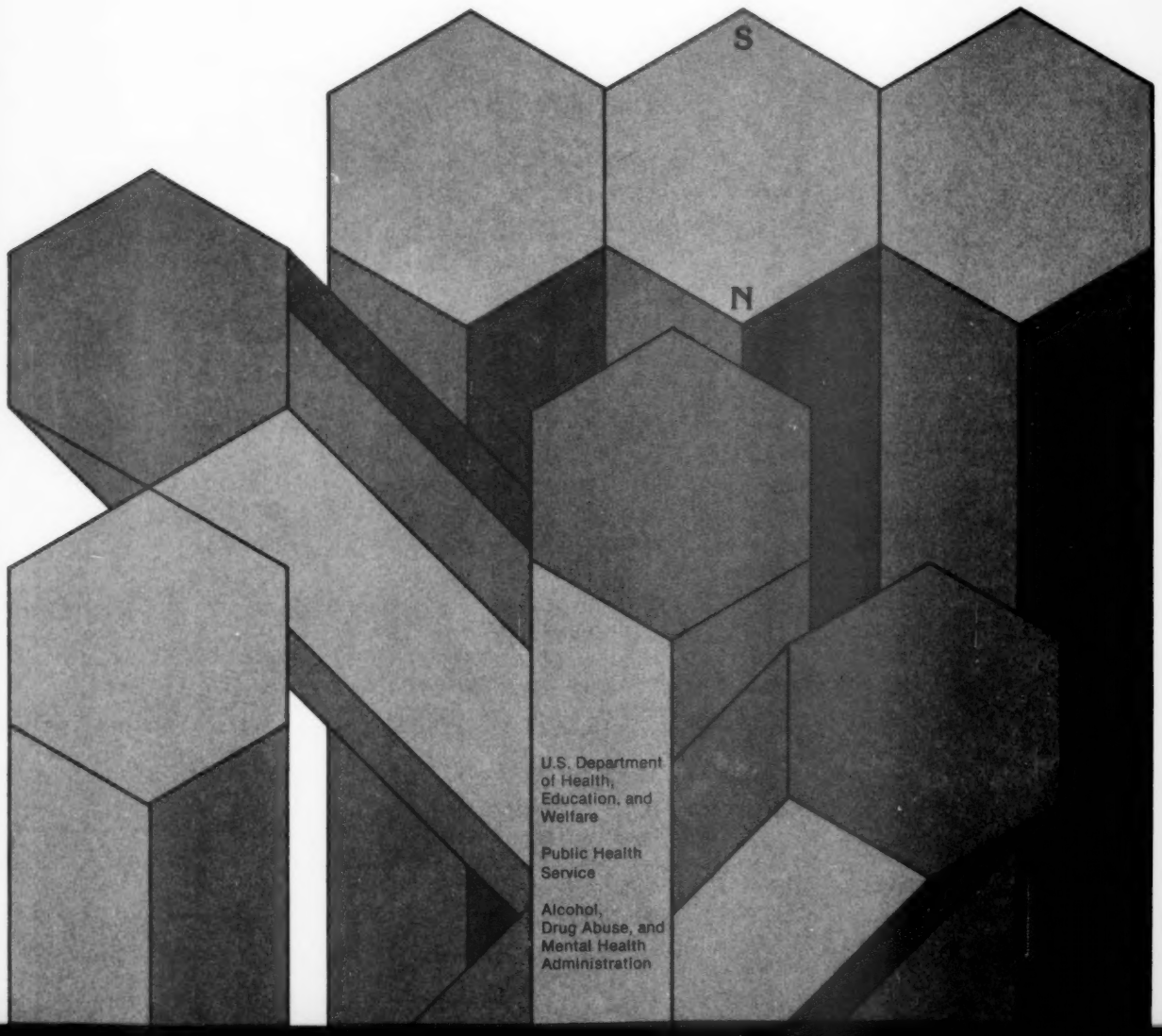
National Institute of Mental Health

The National Clearinghouse for Mental Health Information

VOL. 15 NO. 3 January 1978

Psychopharmacology Abstracts



PSYCHOPHARMACOLOGY ABSTRACTS is a publication of the National Clearinghouse for Mental Health Information of the National Institute of Mental Health. It is a specialized information medium designed to assist the Institute in meeting its obligation to foster and support laboratory and clinical research into the nature and causes of mental disorders and methods of treatment and prevention. Specifically, this information service is designed to meet the needs of investigators in the field of psychopharmacology for rapid and comprehensive information about new developments and research results. For information or correspondence with the National Institute of Mental Health concerning *Psychopharmacology Abstracts*, changes of address, or removal of names from the mailing list see the inside back cover page.

The Secretary of Health, Education, and Welfare has determined that the publication of this periodical is necessary in the transaction of the public business required by law of this Department. Use of funds for printing this periodical has been approved by the Director of the Office of Management and Budget through October 30, 1979.

Volume 15, Number 3 January 1978

CONTENTS

Psychopharmacology Abstracts, is arranged in seventeen categories so that readers may focus more readily on their areas of interest. The Subject and Author Indexes refer the user to the categories under which the abstracts will be found. Thus, in the number 097961 11-14, the first six digits refer to the abstract number, "11" refers to the issue of *Psychopharmacology Abstracts*, and "14" refers to the category.

Carrie Lee Rothgeb, *Editor*
Bette L. Shannon, *Managing Editor*

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service

Alcohol, Drug Abuse, and Mental Health Administration
National Institute of Mental Health
National Clearinghouse for Mental Health Information
5600 Fishers Lane
Rockville, Maryland 20857

DHEW Publication No. (ADM) 78-150
Printed 1978

For sale by the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402. Subscription price per year in the United States, Canada, and Mexico: $14; other countries, $22.50. Single copy $3.50. Index issue $2.10. The Clearinghouse does not sell copies of *Psychopharmacology Abstracts*. Persons wishing to subscribe by the year or to purchase single copies should send their orders, accompanied by check or money order, directly to the Superintendent of Documents.

ABSTRACTS

PRECLINICAL PSYCOPHARMACOLOGY

01 CHEMICAL SYNTHESIS, ISOLATION AND CHARACTERIZATION

002182 Alliez, J. no address /**Therapeutic continuity of the millenia. Justification of the ancient use of veratrum (album) by discoveries of modern psychopharmacology.**/ Continuites therapeutiques millenaires. Justification de l'usage antique de l'ellebore (blanc) par les decouvertes de la psychopharmacologie moderne. Annales Medico-Psychologiques (Paris). 1(2):255-259, 1976.

The historical and contemporary use of Veratrum album in mental disorders was discussed at the January 26, 1976 meeting of the Societe Medico-Psychologique. Veratrum album has sedative, hypotensive, anesthetic, and hypothermic effects, but can cause toxic gastrointestinal and cardiovascular reactions. Hippocrates used the drug for nervous disorders, as did Avicenna. In the middle ages, Veratrum album was used in depression. Veratrum was used in the 18th and most of the 19th century, being removed from the Codex in 1884. Modern research shows Veratrum album to have properties similar to those of reserpine, the chief alkaloid of Rauwolfia serpentina, and therefore Veratrum album was restored to the Codex in 1975. 14 references.

002183 Daudel, Raymond; Esnault, Liliane; Labrid, Claude; Busch, Norbert; Moleyre, Jacques; Lambert, Jean. Centre de Mecanique Ondulatoire Appliquee, 23, rue du Maroc, F-79019 Paris, France **Coordination of quantum chemistry and molecular pharmacology studies in the investigation of a series of disubstituted 1,4-tetrahydro-oxazines.** European Journal of Medicinal Chemistry (Paris). 11(5):443-449, 1976.

The pharmacological in vitro properties and chemical properties of a series of 1,4-tetrahydro-oxazines were studied using quantum chemistry and molecular pharmacology. Electrostatic potential patterns demonstrated certain similarities between one of these compounds (1841 CERM), serotonin (5-HT) and noradrenalin (NA). Pharmacological in vitro investigation revealed that the compounds have an affinity for M and D tryptaminergic receptors and have 5-HT agonist activity. The interaction between 1841 CERM and 5-HT occurred at the level of the receptors. The interaction of this compound with NA was not of a competitive nature, and the analogies observed in the electrostatic patterns were not confirmed pharmacologically. 40 references. (Author abstract modified)

002184 DeLisser-Matthews, Lena A.; Khalaj, Ali. Philadelphia College of Pharmacy and Science, Philadelphia, PA 19104 **Electrochemical evidence for interaction between chlorpromazine hydrochloride and trifluoperazine hydrochloride and the flavin coenzymes.** Journal of Pharmaceutical Sciences. 65(12):1758-1763, 1976.

Polarographic and chronopotentiometric methods were applied to study the effects of the phenothiazine tranquilizers chlorpromazine hydrochloride and trifluoperazine hydrochloride on the electrochemical behavior of the flavin coenzymes flavin mononucleotide and flavin adenine dinucleotide. The effects of the drugs were measured mainly by decreases in the diffusion currents developed in the polarographic experiments and by a similar decrease in the chronopotentiometric constant, in the chronopotentiometric experiments when the coenzymes were reduced in the presence of the added drugs. It is suggested that the observed interference with the redox properties of the coenzymes could conceivably be related to the reported ability of the drugs to inhibit respiration and produce their tranquilizing effect. 14 references. (Author abstract modified)

002185 Neckers, L. M.; Meek, J. L. Laboratory of Preclinical Pharmacology, National Institute of Mental Health, St. Elizabeths Hospital, Washington, D. C. 20032 **Measurement of 5HT turnover rate in discrete nuclei of rat brain.** Life Sciences (Oxford). 19(10):1579-1584, 1976.

Five nonisotopic methods of measuring serotonin turnover rate in vivo were compared in discrete nuclei of rat brain. The concentration of serotonin or 5-hydroxyindoleacetic acid was measured by high pressure liquid chromatography in the raphe nuclei, caudate nucleus and hippocampus of rats at various times after the injection of pargyline, probenecid, RO 4/4602 or alpha-propyldopacetamide. The turnover rate is more rapid in the cell bodies than in axon terminals. 17 references. (Author abstract)

002186 Nichols, David E.; Shulgin, Alexander T. Dept. of Medicinal Chemistry and Pharmacognosy, School of Pharmacy and Pharmacal Sciences, Purdue Univ., West Lafayette, IN 47907 **Sulfur analogs of psychotomimetic amines.** Journal of Pharmaceutical Sciences. 65(10):1554-1556, 1976.

The syntheses and physical properties of 2,5-dimethoxy-4-methylthiophenylethylamine and 2,5-dimethoxy-4-methylthiophenylisopropylamine are described. The latter compound is the fulfur analog of the psychotomimetic phenylisopropylamines 2,4,5-trimethoxyphenylisopropylamine and 2,5-dimethoxy-4-methylphenylisopropylamine wherein the methylthio group replaces a methoxy group or a methyl group, respectively. This compound is predicted to be about 30 times as active as mescaline. 19 references. (Author abstract)

02 DRUG DEVELOPMENT (PRECLINICAL SCREENING)

002187 Artemenko, G. N.; Vikhlyayev, Yu. I.; Kucherova, N. F.; Borisova, L. N. Laboratoriya psikhofarmakologii, Instituta farmakologii AMN SSSR, Moscow, USSR /**Pharmacological action of pyrimidoindole derivatives.**/ Farmakologicheskaya aktivnost' proizovdnykh pirimidoindola. Farmakologiya i Toksikologiya (Moskva). 39(6):651-655, 1976.

The spectrum of psychotropic activity of a number of new pyrimidoindole derivatives and the relation between their chemical structure and activity were studied experimentally, employing tests with white mice usually applied in estimating neuroleptics and tricyclic antidepressants. Results showed: indole derivatives exhibit sedative action; 5-methyl derivatives of pyrimido (3,4-alpha) indole and tetrahydropyrimido (3,4-alpha) indole without substituent in the 2nd position are 5-oxytryptophan antagonists; 2,5-dimethyltetrahydropyrimido (3,4-a) indole derivatives selectively potentiate the central effect of 5-oxytryptophan and display a specific spectrum of action resembling that of antidepressants in a number of tests. The action of these compounds, however, is inferior to that of amitriptyline and pyrasidol. 11 references. (Journal abstract modified)

002188 Berendsen, H.; Leonard, B. E.; Rigter, H. Pharmacology Department, Scientific Development Group, Organon, Oss, The Netherlands **The action of psychotropic drugs**

on DOPA induced behavioural responses in mice. Arzneimittel-Forschung (Aulendorf). 26(9):1686-1689, 1976.

Dopa potentiation was used as a screening test for antidepressants in female Charles River mice, weighing 19 to 20g. The mice were pretreated with iproniazid 17 hr before the test, injected i.p. with either the test compound, the reference compound (imipramine), or placebo 1 hr before the test, and given dopa 30 min before the test. Locomotor activity of the mice was rated after administration of dopa. In other mice, the brains were removed 30 min after dopa and were analyzed for norepinephrine, dopamine, serotonin, tyrosine, tryptophan, and GABA. Imipramine increased locomotor activity, as did amitriptyline, mianserin (Org-GB 94), and 5-methylaminoacetyl-6-methyl-5,6-dihydrophenanthridine HCl (Org-OI-77). Chlordiazepoxide and meprobamate potentiated the locomotor effect of dopa, but diazepam and amobarbital did not. Chlorpromazine and haloperidol inhibited dopa induced locomotion. Apomorphine, d-amphetamine, methysergide, and atropine potentiated the dopa effect. Iproniazid plus dopa decreased brain tyrosine, and imipramine, Org-GB 94, chlordiazepoxide, apomorphine, d-amphetamine, chlorpromazine, and diazepam all prevented this decrease. Dopa caused a 300% increase in brain norepinephrine, which was further increased by Org-GB-94. The 75% increase in brain dopamine caused by dopa was potentiated by imipramine, Org-GB-94, chlordiazepoxide, and chlorpromazine. Dopa did not cause an increase in brain tryptophan levels and neither did any drug given with dopa. Dopa alone did not alter brain serotonin levels, but dopa with imipramine, Org-GB-94, chlordiazepoxide, diazepam, and amphetamine caused an increase in serotonin. Dopa did not alter GABA levels; neither did dopa in combination with any drug except amphetamine. It is concluded that the dopa potentiation test does not screen for antidepressants. 15 references.

002189 Costall, Brenda; Naylor, Robert J.; Pinder, Roger M. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, West Yorkshire, England **Hyperactivity induced by tetrahydroisoquinoline derivatives injected into the nucleus accumbens.** European Journal of Pharmacology (Amsterdam). 39(1):153-160, 1976.

The ability of a number of derivatives of tetrahydroisoquinoline to mimic the effects of catecholamines, especially dopamine, in the nucleus accumbens was investigated in the rat. Several derivatives of tetrahydroisoquinoline were injected bilaterally into the nucleus accumbens of rat 2 hr after a nialamide pretreatment and activity recorded in cages fitted with photocells. 2-Methyl-1,2,3,4-tetrahydroisoquinoline amd 2-methyl-6,7-dihydroxy-1,2,3,4-tetrahydroisoquinoline caused only modest hyperactivity responses. However, 3-methyl-6,7-dihydroxy-1,2,3,4-tetrahydroisoquinoline and 3-methyl-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline markedly increased activity in a dose dependent manner. The 3-methyl-6,7-methylenedioxy derivative was most active and equalled the effectiveness of dopamine. The responses to dopamine and to 3-methyl-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline developed within 1 to 2 hr and persisted for at least 6 hr. The hyperactivity induced by dopamine was antagonized in a dose dependent manner by haloperidol; propranolol and aceperone were without effect. Similar results were obtained for these blocking agents against the responses to 3-methyl-6,7-methylenedioxy-1,2,3,4-tetrahydroisoquinoline and 2-methyl-1,2,3,4-tetrahydroisoquinoline but aceperone and propranolol, in addition to haloperidol, were shown to inhibit the hyperactivity induced by 3-methyl-6,7-dihydroxy-1,2,3,4-tetrahydroisoquinoline. 23 references. (Author abstract modified)

002190 DeSantis, Frank, Jr.; Nieforth, Karl A. Vick Divisions Research, Vick Chemical Co., Mt. Vernon, NY 10553 **Synthesis of potential mescaline antagonists.** Journal of Pharmaceutical Sciences. 65(10):1479-1484, 1976.

Potential mescaline antagonists, including 1-(2-(3,4,5-trimethoxyphenyl)ethyl)-3-pyrroline(X), 2-(3,4,5-trimethoxybenzyl)-1,2,3,6-tetrahydropyridine(XI) N-n-propylmescaline(IV), N-cyclopropylmethylmescaline(V) and N-allymescaline(VI) were synthesized and their effects on conditioned mouse swim behavior and on mescaline induced disruptions of conditioned mouse swim behavior were studied. Compounds X and XI produced disruptions in swim behavior and had no effect on the mescaline induced disruptions. Compounds IV, V, and VI did not disrupt swim behavior. Compounds IV and V reduced, and compounds VI antagonized, the mescaline induced disruptions of behavior. 15 references. (Author abstract modified)

002191 Gale, Karen N.; Guidotti, A. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **GABA-mediated control of rat neostriatal tyrosine hydroxylase revealed by intranigal muscimol.** Nature (London). No. 5579:691-693, 1976.

To determine if a reduced release of GABA from descending inhibitory neurons in the striatonigral pathway may occur as a result of a neuroleptic blockade of caudate-putamen(CD)-dopamine (DA) receptors, activating CP-tyrosine hydroxylase (TH) as a result of decreased GABAergic inhibitory control of nigral DA neurones; muscimol was injected directly into the substantia nigra (SN) of rats. The rats were sacrificed and a TH assay was undertaken, a comparison of data with results of data from rats given intranigral bicuculline suggest that muscimol effects are attributable to a specific GABAmimetic effect. Further tests comparing bicuculline effects with those of muscimol and haloperidol on TH activity indicated that GABA receptors probably mediate the activity of muscimol in the SN. It is concluded that it is possible to interfere with haloperidol induced activation of CP-TH by pharmacologically maintaining the functional effect of GABA on nigral neurones and that application of muscimol directly into the nigra acted to preclude the influence of a striatonigral feedback pathway. This implies that a decrease in GABA release in nigra is required for neuroleptic induced activation of CPTH. 22 references.

002192 Loew, D. M.; Vigouret, J. M.; Jaton, A. L. Sandoz Ltd., Biological and Medical Research Division, CH-4002, Basel, Switzerland **Neuropharmacological investigations with two ergot alkaloids, Hydergine and bromocriptine.** Postgraduate Medical Journal (Oxford). 52(Supplement 1):40-46, 1976.

In a paper presented at a symposium on ergot compounds in London in May 1975, neuropharmacological investigations wtih hydergine and bromocriptine were reported which indicate that the two ergot alkaloids possess different actions on the central nervous system. Hydergine enhanced excitability in mice but did not induce overt motor stimulation or stereotypies in mice or rats. It altered the sleep/wakefulness cycle of the rat by prolonging wakefulness and by shortening classical and paradoxical sleep. In the rabbit, hydergine counteracted antinociceptive effects of morphine, possibly by a dopamine agonist effect in the pontomedullary region. Bromocriptine induced long-lasting motor stimulation and stereotypies in mice and rats. In rats lesioned unilaterally with 6-hydroxydopamine in the substantia nigra it induced contralateral turning. In the rabbit, an antagonism of morphine induced antinociception was observed which appeared to depend on a dopamine

agonist action in the area close to the striate nucleus. Hydergine exerts complex effects on the central nervous system which are different from those of known central stimulants. The results suggest that it might act as a dopamine agonist at the level of the pontomedullary reticular formation. Bromocriptine appears to be a long-acting dopamine agonist with a main site of action in the extrapyramidal system. 27 references. (Author abstract)

002193 Pert, Candace B.; Pert, Agu; Chang, Jaw-Kang; Fong, Bosco T. W. Section on Biochemistry, Adult Psychiatry Branch, NIMH, Bethesda, MD 20014 **(D-Ala2)-Met-enkephalinamide: a potent, long-lasting synthetic pentapeptide analgesic.** Science. 194(4262):330-332, 1976.

The synthesis of a novel pentapeptide, designed and detected by in vitro analysis, which elicits a potent, long-lasting analgesia is reported. (D-Ala2)-Met-enkephalinamide (DALA) was found to bind to opiate receptors almost as tightly as methionine-enkephalin. It was shown to be a potent analgesic in three rat tasks: the tail flick procedure; the flick jump task; and in reactions to pinches of limbs with forceps. Since DALA, which is not susceptible to degradation by brain enzymes, is almost as potent and long-lasting as morphine, it provides a useful tool for studying behavioral effects of opiate peptides. 24 references. (Author abstract modified)

002194 Randrup, Axel; Mogilnicka, Ewa. St. Hans Hospital, Roskilde, Denmark **Spectrum of pharmacological actions on brain dopamine. Indications for development of new psychoactive drugs: discussion of amantadines as examples of new drugs with special actions on dopamine systems.** Polish Journal of Pharmacology and Pharmacy (Warsaw). 28:551-556, 1976.

Biochemical and behavioral preliminary research of the psychoactive drugs, amantadine (D1) and 1,3-dimethyl-5-aminoadamantane (D145) is reviewed with particular emphasis on their dopaminergic actions. D1 or D145 decreased significantly apomorphine or amphetamine induced stereotypy in rats but in experiments with chronic pretreatment with amantadines potentiation of stereotypy was observed. D145 (20mg/kg) abolished stereotypy in these conditions. In biochemical experiments D1 or D145 were neither like apomorphine nor like amphetamine. Its concluded that D1 and D145 in addition to their amine releasing properties have the ability to partially occupy the dopaminergic receptor. 33 references. (Author abstract modified)

002195 Slater, I. H.; Jones, G. T.; Moore, R. A. Pharmacological Research, Lilly Research Laboratories, Indianapolis, IN 46206 **Depression of REM sleep in cats by nisoxetine, a potential antidepressant drug.** Psychopharmacology Communications. 2(3):181-188, 1976.

Investigations on the effects of nisoxetine hydrochloride as a potential antidepressant were undertaken. Nisoxetine hydrochloride, a potent and specific inhibitor of norepinephrine uptake, suppressed REM sleep in cats. Oral doses as small as 0.1mg/kg were effective during the first 2 1/2 hours of a recording session; 0.25mg/kg, for 5 hours. The amount of slow wave sleep increased in cats that received 0.1to 1.0mg/kg of nisoxetine. These changes in sleep pattern resemble those reported after treatment with somewhat higher doses of tricylic antidepressants. 7 references. (Author abstract)

002196 Sowell, J. Walter, Sr.; Blanton, C. DeWitt, Jr. School of Pharmacy, University of South Carolina, Columbia, SC 29208 **New synthesis of substituted pyrrolo(1,2-a)(1,3)diazepine and its pharmacological activity.** Journal of Pharmaceutical Sciences. 65(6):908-910, 1976.

A new route for the synthesis of the substituted pyrrolo(1,2-a)(1,3)diazepine nucleus from readily available precursors and a description of the pharmacological activities of the compound in animals are reported. The compound was tested for antimalarial activity in mice, antineoplastic activity in mice, acute hypotensive activity in rats and dogs, effect on cholesterol/lipoprotein levels in rats, antiinflammatory activity in rats, antiviral activity in mice, CNS depressant or stimulant activity in mice, diuretic activity in fasted rats, and antidiabetic activity in rats. Hypotensive activity of relatively short duration was observed in rats. The compound lacked positive pharmacological activity in the remaining tests. 20 references. (Author abstract modified)

03 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

002197 Aaseth, Jan. Institute of Clinical Biochemistry, University of Oslo, Rikshospitalet, Oslo 1, Norway **Mobilization of methyl mercury in vivo and in vitro using N-acetyl-DL-penicillamine and other complexing agents.** Acta Pharmacologica et Toxicologica (Kobenhavn). 39(3):289-301, 1976.

The distribution and excretion of mercury was studied in mice given a single intravenous dose of methylmercuric chloride. Oral treatment with N-acetyl-DL-penicillamine removed more mercury from the brain and from the whole body than the corresponding treatment with other complexing agents, and it was also effective on delayed treatment. In vitro experiments showed that the chemical affinity of N-acetyl-DL-penicillamine for methylmercury was higher than that of the other thiols tested, except D-pencillamine. In contrast to the latter, N-acetyl-DL-penicillamine easily penetrated the cellular membranes, and therefore rapidly removed a substantial fraction of methylmercury from the blood cells. It is concluded that N-acetyl-DL-penicillamine can reduce the mercury concentration in brain cells by converting the intracellularly non-diffusible methylmercury into a freely diffusible complex. 28 references. (Author abstract modified)

002198 Aaseth, Jan; Wannag, Axel; Norseth, Tor. Institute of Clinical Biochemistry, University of Oslo, Rikshospitalet, Oslo 1, Norway **The effect of N-acetylated DL-penicillamine and DL-homocysteine thiolactone on the mercury distribution in adult rats, rat fetuses and Macaca monkeys after exposure to methyl mercuric chloride.** Acta Pharmacologica et Toxicologica (Kobenhavn). 39(3):302-311, 1976.

The distribution and excretion of mercury was studied in pregnant rats, given a single intravenous dose of CH3203HgCl on the 13th day of pregnancy. Oral treatment for one week with N-acetyl-DL-penicillamine increased the mercury excretion in feces and urine. Such treatment mobilized mercury from all the organs tested, and the fetal and maternal brain levels of mercury were decreased to 20% and 33% of the controls, respectively. The rapid removal of metal deposits following treatment with N-acetyl-DL-penicillamine is attributed to a free penetration of the complexing thiol into the tissue cells in question. No signs of toxicity were detected in monkeys given an effective daily dose of the agent for 6 days. In contrast N-acetyl-DL-homocysteine thilactone was found to be toxic in the monkeys. In addition, the latter agent was ineffective in increasing the mercury elimination from the brains of monkeys, rats, and rat fetuses. 17 references. (Author abstract modified)

002199 Ahtee, Liisa. School of Pharmacy, Department of Pharmacology, University of Helsinki, Kirkkokatu 20, SF-00170 Helsinki 17, Finland **Effect of cholinergic drugs on methadone-induced catalepsy and stereotypies in rats treated chronically with methadone.** European Journal of Pharmacology (Amsterdam). 39(2):203-213, 1976.

The effects of antimuscarinic (atropine, scopolamine, methylscopolamine), muscarinic (RS86, pilocarpine), antinicotinic (mecamylamine, hexamethonium) and nicontinic chlolinergic drugs on the catalepsy and stereotypies induced by acute methadone in rats treated chronically with methadone were studied. The antimuscarinic drugs potentiated and the muscarinic drugs antagonized the cataleptic effect of methadone, the antimuscarinic drugs tended to antagonize and the muscarinic drugs potentiated the methadone induced stereotypies. Nicotine initially slightly potentiated, and mecamylamine antagonized the cataleptic effect of methadone. Results show that the effects of antimuscarinic and muscarinic drugs on the catelepsy and stereotypies induced by methadone are opposite to their effects on the catalepsy and stereotypies produced by drugs which are thought to act on the postsynaptic dopaminergic receptors. 40 references. (Author abstract modified)

002200 Akaike, Akinori; Kawasaki, Kazuo; Doi, Takayuki; Takagi, Hiroshi. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyoto University, Kyoto 606, Japan **Effect of morphine microinjection into the medulla oblongata on the spinal dorsal horn neuron.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):119P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March 1976, a study of the effects of microinjection of morphine into the nucleus reticularis gigantocellularis (nRgc) of the medulla oblongata was reported. Morphine injected into the nRgc inhibited the bradykinin activated unit activities of the lamina V neuron of the spinal dorsal horn of the rabbit. This effect was antagonized by injection of naloxone into the same site. Naloxone alone produced no effect on the neuron. Microinjections of morphine into the nRgc also produced analgesic effects as determined using the tail pinch method in rats. These effects were antagonized by subcutaneous administration of naloxone. It is suggested that the nRgc and adjacent structures may be sites for the analgesic action of morphine. (Author abstract modified)

002201 Akimov, Yu. A. Institut fiziologii im. A. A. Bogomol'tsa AN USSR, Kiev, USSR /**Effect of sodium amytal on electrophysiological properties of snail giant neurons.**/ Vliyaniye amitala natriya na elektrofiziologicheskiye svoystva gigantskikh neyronov vinogradnoy ulitki. Neyrofiziologiya (Kiev). 8(3):322-324, 1976.

Effects of sodium amytal on electrophysiological properties of giant neurons of snails were studied with the use of microelectrodes. Sodium amytal increased the resting potential, while decreasing and finally eliminating action potentials, and temporarily decreased the input resistance of the neuron membrane. The intracellular potassium content decreased, but sodium content remained practically unchanged. It is suggested that these effects are connected with changes in the membrane's potassium permeability and with disturbances in the mechanisms of action potential generation. 9 references.

002202 Anden, Nils-Erik; Grabowska, Maria. Department of Pharmacology, University of Goteborg, Fack, S-40033 Goteborg 33, Sweden **Pharmacological evidence for a stimulation of dopamine neurons by noradrenaline neurons in the brain.** European Journal of Pharmacology (Amsterdam). 39(2):275-282, 1976.

The effects of yohimbine, phenoxybenzamine, and clonidine on the synthesis and the utilization of dopamine and noradrenaline in the central nervous system of rats were investigated. Dopa accumulation following decarboxylase inhibition and the alpha-methyltyrosine induced disappearance of the amines were used as the measure of these effects. The synthesis and utilization of dopamine and noradrenaline were accelerated by yohimbine. Clonidine plus phenoxybenzamine inhibited the synthesis and utilization of dopamine and the combination also partly antagonized the effects of yohimbine on the turnover of dopamine. This hypothesis is supported by the findings that yohimbine and phenoxybenzamine did not change the increased synthesis of dopamine in reserpine treated rats and that clonidine did not inhibit the increased synthesis of dopamine after axotomy or treatment with reserpine. 28 references. (Author abstract modified)

002203 Arefolov, V. A.; Panasyuk, P. V.; Pidevich, I. N. Laboratorii farmakologii nervnoy sistemy, Instituta farmakologii AMN SSSR, Moscow, USSR /**Sympathomimetic effect of serotonin and action of imipramine and phthoracizine on this effect.**/ Simpatomimeticheskiy effekt serotonina i vliyaniye na nego imipramina i ftoratsizina. Farmakologiya i Toksikologiya (Moskva). 39(6):672-675, 1976.

The sympathomimetic effect of serotonin and the action of imipramine and phthoracizine on this effect were studied in dogs. Serotonin was shown to lower the content of norepinephrine in the sympathetic nerves and synaptic vesicles of adrenergic fibers in the vas deferens. Imipramine, and to a lesser degree phthoracizine, lessened the ability of serotonin to liberate norepinephrine from sympathetic endings. 9 references. (Journal abstract)

002204 Arushanyan, E. B.; Belozertsev, Yu. A.; Karpov, V. N. Chitinskiy meditsinskiy institut, Chita, USSR /**Some characteristics of amphetamine stereotypy as a drug model of psychopathology.**/ Nekotorye osobennosti fenaminovoy stereotipii kak lekarstvennoy modeli psikhopatologii. Zhurnal Nevropatologii i Psikhiatrii Imeni S. S. Korsakova (Moskva). 76(8):1214-1218, 1976.

The effects of 2 to 6mg/kg ip amphetamine and 40 to 60mg/kg ip caffeine on stereotyped movements were studied in 12 cats. Amphetamine caused stereotyped movements accompanied by crude disorders of conditioned avoidance with an increase in intrasignal reactions, weakening of differentiated inhibition, and inhibition of avoidance responses caused by low frequency stimulation of the caudate nucleus, whereas caffeine had none of these effects. It appears that many of the indices of amphetamine stereotypy may be explained by disturbances of the filtering and retention functions of the caudate nucleus. 26 references.

002205 Asnina, V. V.; Andreyeva, N. I. Vesesoyuznyy nauchno-issledovatel'skiy khmiko-farmatsevticheskiy institut im S. Ordzhonikidze, Moscow, USSR /**Effect of pyrazidol on the endogenous norepinephrine level in rat brain and heart tissue.**/ Vliyaniye pirzidola na soderzhaniye endogennogo noradrenalina tkanyakh mozga i serdtsa krys. Farmakologiya i Toksikologiya (Moskva). 39(6):682-684, 1976.

A preclinical test was made of the new Soviet antidepressant pyrazidol, 1, 10-trimethylene-8-methyl-1,2,3,4-tetrahydropyrazino(1,2-alpha) indole, in rats. When given in single doses of 25mg/kg and 50mg/kg i.p. and in a dose of

24mg/kg for 10 days, the new drug had no effect on the norepinphrine content of the brain, and only slightly increased the norepinephrine level in heart tissue. 5 references.

002206 Avakyan, R. M.; Arushanyan, E. B. Dept. of Pharmacology, Medical Inst., Chita, USSR **Effect of catecholaminergic drugs on epileptogenic properties of the caudate nucleus.** Neuroscience and Behavioral Physiology. 7(1):13-16, 1976.

The effect of catecholaminergic drugs on epileptogenic properties of the caudate nucleus was investigated. Drugs stimulating cathecholaminergic transmission (dopa, apomorphine, amphetamine, and their combination with disulfiram) weakened the epileptogenic properties of the caudate nucleus in freely moving rats. Under the influence of these drugs the cortical electroencephalographic response to single stimulation of the nucleus was shortened in animals receiving subconvulsant doses of leptazol and the intensity of the spike wave rhythm bound with repeated caudate stimuli was reduced. Conversely, inhibitors of catecholaminergic transmission (chlorpromazine, haloperidol, alpha-methyltyrosine, and disulfiram) potentiated the epileptogenic effects of the caudate nucleus. 6 references. (Journal abstract modified)

002207 Barnard, Eric A.; Bhargava, Arvind K.; Hudecki, Michael S. Department of Biochemistry, Imperial College, London SW7, England **Postponement of symptoms of hereditary muscular dystrophy in chickens by 5-hydroxytryptamine antagonists.** Nature (London). 263(5576):422-424, 1976.

Evidence that 5-hydroxytryptamine (5-HT) is involved in some way in the development of the symptoms of muscular dystrophy, and that administration of a 5-HT antagonist, methysergide, retards the development of the symptoms is discussed. The effect is more general, in that a second antiserotoninergic drug of entirely different chemical structure, cyproheptadine, is also effective. A combination of the two agents is also beneficial. For all cases a highly significant difference was found between the untreated and the treated groups. The results suggest that an investigation of a range of 5-HT antagonists could be of therapeutic interest and might provide a clue to one of the determinants of the dystrophic process. 12 references.

002208 Bartmus, D.; Gumulka, S. W.; Dinnendahl, V.; Schonhofer, P. S. Department of Pharmacology, Medizinische Hochschule Hannover, Karl-Wiechert-Allee 9, D-3000 Hannover 61, Germany **Brain cyclic nucleotides and adrenolytics: effects on amphetamine and apomorphine induced changes.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 294(Supplement):R11, 1976.

In a paper presented at a pharmacology meeting in Hannover, Germany, on September 14-17, 1976, the effects of amphetamine (AM) and apomorphine (AP) induced changes on cGMP content in the cerebellum and medial forebrain of the mouse are investigated. Pretreatment with alpha-adrenolytics (phentolamine 10mg/kg) reduced the increase in cGMP levels elicited by AM in both parts of the brain. Similar effects were obtained following stimulation by AP. Pretreatment with beta-adrenolytics (bunitrolol 2mg/kg) did not affect the AM and AP induced rise in cGMP. Low doses of clonidine in cGMP content in both parts of the brain and significantly diminished the effects of both AM and AP. A high dose of clonidine alone (2.5mg/kg) produced a biphasic effect on cGMP levels in both parts of the brain initially a pronounced decrease followed by a moderate elevation above controls. During the initial phase the effects of AM and AP were markedly diminished or even abolished. Results indicate that beta-adrenergic effects are not involved in stimulation of cGMP levels in the brain. It is concluded that in view of the inhibitory effect of phentolamine the action of clonidine may be interpreted as that of an inhibitor with high intrinsic activity. (Author abstract modified)

002209 Belmaker, Robert H.; Ebstein, Richard P.; Schoenfeld, Helen; Rimon, Ranan. Jerusalem Mental Health Center, Ezrath Nashim, P.O.B. 140, Jerusalem, Israel **The effect of haloperidol on epinephrine-stimulated adenylate cyclase in humans.** Psychopharmacology (Berlin). 49(2):215-217, 1976.

The effects of lithium and haloperidol on the epinephrine induced increase in plasma cyclic adenosine monophosphate (cyclic AMP) levels was investigated in healthy humans. Therapeutic doses of lithium block the epinephrine induced rise in plasma cyclic AMP levels, suggesting that lithium inhibits beta-adrenergic adenylate cyclase. Haloperidol, a drug also effective in the treatment of mania, produces a mean rise in plasma cyclic AMP levels after epinephrine administration; the magnitude of the response is the same as for controls. These findings are discussed in relation to the possible pharmacological mechanisms of action of lithium and haloperidol in the control of manic-depressive illness. 18 references. (Author abstract modified)

002210 Berti, F.; Bernareggi, V.; Folco, G. C.; Fumagalli, R.; Paoletti, R. Institute of Pharmacology and Pharmacognosy, University of Milan, I-20129 Milan, Italy **Prostaglandin E2 and cyclic nucleotides in rat convulsions and tremors.** Advances in Biochemical Psychopharmacology. 15:367-377, 1976.

Studies carried out in rats to determine whether the anticonvulsant effects of prostaglandin-E2 (PGE2) toward pentamethylene tetrazol (PMT) induced convulsions are reflected by changes in cerebellar cyclic nucleotides, i.e. cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP) are reported. The convulsant effect of PMT was correlated with cyclic nucleotide concentrations. The rise of cGMP occurred within 30 sec after PMT administration, and the rise of cAMP occurred only after the onset of convulsions. Subconvulsant doses of PMT increased cerebellar cGMP but not cAMP. The protective activity of PGE2 was compared with that of chlordiazepoxide (CDP), and anticonvulsant benzodiazepine. Both PGE2 and CDP prevented convulsions and the increase of cerebellar cAMP. PGE2 inhibited the increase of cGMP without affecting its basal concentrations, while CDP decreased the basal levels of cGMP and limited, but did not prevent, the PMT induced increase of cGMP concentration. It was also found that PGE2 prevents both the tremors and the rise of cerebellar cGMP induced by harmaline. It is suggested that PGE2 and CDP exert their anticonvulsant effects at different sites and/or by different mechanisms. It is speculated that PGE2 acts at the synaptic link between climbing fibers and Purkinje cells, but that an indirect effect associated with the cardiovascular effects of the compound cannot be ruled out. 38 references.

002211 Biggio, G.; Costa, E.; Guidotti, A. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Different mechanisms mediating the decrease of cerebellar cGMP elicited by haloperidol and diazepam.** Advances in Biochemical Psychopharmacology. 15:325-335, 1976.

Studies of the effects of various drugs, including harmaline, 3-acetylpyridine, isoniazid, and apomorphine on cerebellar cyclic guanosine monophosphate (cGMP) content which indicate that cGMP is a biochemical marker of climbing

(adrenergic) fiber and mossy fiber activity are reviewed, and studies of the mechanisms by which haloperidol and diazepam modulate cerebellar cGMP content are reported. The actions of haloperidol and diazepam on the increases in cerebellar cGMP induced by harmaline, isoniazid, and apomorphine were compared. It was found that: 1) doses of diazepam too small to change cGMP content prevented the apomorphine induced increase in cGMP, but a dose of haloperidol (which itself decreased cGMP) did not antagonize the effect of apomorphine; 2) diazepam abolished the increase in cerebellar cGMP induced by isoniazid, but large doses of haloperidol did not; 3) doses of diazepam which decreased the cerebellar cGMP content reduced the harmaline induced increase in cGMP, while haloperidol was much less effective in reducing the effect of harmaline; and 4) premedication with a cholinolytic agent decreased the haloperidol induced reduction in cGMP content but not that of diazepam. The effects of these drugs on apomorphine induced stereotyped behavior, harmaline induced tremor, and latency of isonizid induced convulsions also differ at the dose levels tested. It is posited that diazepam and haloperidol decrease cerebellar cGMP by different mechanisms, which are described and discussed. 23 references.

002212 Biggio, G.; Costa, E.; Guidotti, A. Department of Pharmacology, University of Cagliari Medical School, Cagliari, Italy **A cerebellar model to study the actions of diazepam and muscimol on gamma aminobutyric acid mediated transmission. (Unpublished paper).** Washington, DC, NIMH, 1976. 18 p.

To investigate the activity of four drugs that reduce 3′,5′-cyclic guanosine monophosphate (cGMP) in the cerebellar cortex, male rats were parenterally injected with either muscimol, morphine, diazepam or haloperidol. By using a series of experimental designs it was shown that morphine and haloperidol lower cerebellar cGMP by acting on specific striatal receptors. The activation of opiate and dopamine and the inhibition of dopamine receptors decrease the afferent excitatory input to pontine nuclei which results in a decreased activity of mossy fibers, originating from cell bodies in the pontine nucleus, which reduce cGMP content in cerebellar cortex. In contrast, diazepam and muscimol lower cGMP by activating GABA receptors. While muscimol is a direct agonist, diazepam effect occurs in the presence of a limiting amount of cerebellar GABA and may involve a synergistic action with the endogenous agonist. The molecular nature of this synergism is being investigated. 34 references. (Author abstract modified)

002213 Breakefield, Xandra O.; Giller, Earl L., Jr. Department of Human Genetics, Yale University School of Medicine, New Haven, CT 06510 **Neurotransmitter metabolism in cell culture.** Biochemical Pharmacology (Oxford). 25(21):2337-2342, 1976.

A portion of the literature dealing with the study of the nervous system using cell culture techniques is reviewed. Methods for the culture of neural cells and glial cells are discussed. Other topics presented include results of studies dealing with: 1) the various aspects of neurotransmitter metabolism examined in culture, including uptake, storage, synthesis, degradation, release and membrane reception; 2) the regulation of neurotransmitter synthesis; 3) the roles of acetylcholine and cholinergic receptors in the formation of cholinergic synapses; 4) the developmental sequence of growth of noradrenergic neurones; 5) the responses of cultured nerve cells to drugs and neurotransmitters and the molecular mechanisms of action of drugs; and 6) the use of mutant or epigenetic variant cells to study altered neurotransmitter metabolism. 107 references.

002214 Breyer, Ursula; Junginger, Wilfried; Villumsen, Deborah. Institute of Toxicology, University of Tubingen, D-74 Tubingen, Germany **Phenobarbital-induced prolongation of half-life and alteration of distribution of a phenothiazine drug metabolite in the rat.** Biochemical Pharmacology (Oxford). 25(23):2623-2629, 1976.

The effect of phenobarbital on the half-life of the perazine metabolite N-/gamma-(phenothiazinyl-10)-propyl/-ethylenediamine (PPED) was studied in male Wistar rats weighing 240 to 300gm. Concomitant administration of phenobarbital altered the distribution of PPED and other perazine metabolites, leading to higher concentrations in the liver and lower concentrations in the kidney and brain. Both PPED and SKF 525A caused desmethylperazine to be converted to PPED to a smaller extent. Phenobarbital retarded elimination of a single oral dose of PPED from the liver and kidney, whereas p,p′DDT slightly enhanced the decline of PPED tissue levels. The phenobarbital induced and DDT induced increases of cytochrome P-450 were not abolished by PPED; neither did PPED abolish the phenobarbital induced and DDT induced increases in ethylmorphine demethylation in rat liver microsomes. It is concluded that phenobarbital treatment increased PPED binding to liver cell constituents and thus reduces its availability for distribution to extrahepatic organs and for metabolism. 30 references.

002215 Burkard, W. P.; Pieri, L.; Haefely, W. F. Hoffmann-La Roche & Co. Ltd, Department of Experimental Medicine, CH-4002 Basel, Switzerland **Changes of rat cerebellar guanosine 3′,5′-cyclic phosphate by dopaminergic mechanisms in vivo.** Advances in Biochemical Psychopharmacology. 15:315-324, 1976.

The effects of dopamine receptor stimulation via apomorphine or lysergic acid diethylamide (LSD) on the cyclic guanosine monophosphate (cGMP) content of rat cerebellum was studied. Apomorphine produced a dose dependent increase of cGMP in the cerebellum. Haloperidol and scopolamine completely prevented this increase, and reserpine reduced the increase by 50%. LSD elevated cerebellar cGMP, and this effect was also abolished by haloperidol. It is suggested that the primary site of action of the drugs is the caudate nucleus, from which two neuronal pathways could trigger the increase of cGMP in the cerebellum. 37 references.

002216 Butcher, S. H.; Cho, A. K. Department of Pharmacology, School of Medicine, University of California, Los Angeles, CA 90024 **Modulation of acetylcholine in the neostriatum by dopamine and 5-hydroxytryptamine.** Proceedings of the Western Pharmacological Society. 19:130-135, 1976.

To extend previous studies suggesting that both dopamine (DA) and 5-hydroxytryptamine (5-HT) have an excitatory effect on cholinergic interneurons in the neostriatum, and to examine pharmacologically the dynamics of the monoaminergic/cholinergic interactions in the neostriatum, the effects of dopaminergic and serotonergic agonists and antagonists on striatal acetylcholine (ACh) levels and synthesis were investigated. It was found that pimozide produced a decrease in steady state ACh and a decrease in labelled ACh levels, suggesting that pimozide caused a decrease in ACh turnover, consistent with a blocking of excitatory DA influences on cholinergic interneurons in the neostriatum. Similarly, the marked reduction in the amount of labelled ACh formed after p-chloroamphetamine suggested a decrease in ACh turnover in the neostriatum as a consequence of 5-HT depletion. The increase in labelled ACh in the neostriatum after 5-HTP administration suggests an increase in ACh turnover, consistent with

the lesion data of Butcher et al. The effects of the drugs tested are more easily compared with lesions of the 5-HT or DA projections to the neostriatum due to the relative selectivity of these drugs, whereas the lack of specificity of L-DOPA may account for the apparent incompatibility of data from this precursor with the results in Butcher. 20 refernces. (Author abstract modified)

002217 Campbell, I. C.; Colburn, R.; Walker, M. N.; Lovenberg, W.; Murphy, D. S. Section on Clinical Neuropharmacology, National Institute of Mental Health, Bethesda, MD 20014 **Norepinephrine and serotonin metabolism in the rat brain: effects of chronic phenelzine administration. (Unpublished paper).** Rockville, MD, NIMH, 1976. 15 p.

The effects of acute and chronic phenelzine treatment on 5-hydroxytryptaminergic (5-HT, serotonin) neurones and noradrenergic neurones in the rat brain were studied. Tryptophan uptake was increased after a single dose of the drug. After 7 days and 14 days of treatment, increased uptake of tyrosine was the only significant change observed but after 21 days, norepinephrine (NE) uptake was significantly decreased. Monoamine oxidase activity decreased linearly during the phenelzine treatment, reaching 5% of control values at 21 day. Endogenous levels of NE and 5-HT increased after one injection of phenelzine, but over 21 days, there was an adaptive response and amine values returned towards control levels. Phenelzine had no effect on tyrosine hydroxylase activity, but significantly increased trytophan hydroxylase activity. 45 references. (Author abstract modified)

002218 Carrara, M. C.; Baines, A. D. Department of Clinical Biochemistry, Banting Institute, University of Toronto, Toronto, Ontario M5G 1L5, Canada **Propranolol induces acute natriuresis by beta blockade and dopaminergic stimulation.** Canadian Journal of Physiology and Pharmacology (Ottawa). 54(5):683-691, 1976.

Blockage of beta receptors and dopaminergic stimulation were studied in diuretic and nondiuretic rats pretreated with dl-propranolol in a study of some of the ways through which propranolol might increase sodium excretion by normal animals. dl-Propranolol produced a transient twofold to threefold increase in sodium excretion in nondiuretic rats infused with Pitressin and aldosterone and in water diuretic rats. Sodium excretion increased more in rats depleted of renin by chronic Doca and salt administration than in rats maintained on a low salt diet. An angiotensin inhibitor (1,sarcosine-8,valine angiotensin II) decreased sodium excretion. Therefore, the natriuresis was not mediated by antidiuretic hormone, aldosterone, or renin-angiotensin. d-Propranolol did not produce a natriuresis. Prior treatment with phenoxybenzamine did not prevent the natriuretic response but chlorisondamine pretreatment did. The natriuresis is produced by beta blockade and requires postganglionic nerve function, but is independent of alpha receptors. dl-Propranolol decreased heartrate and cardiac output, but systemic pressure did not fall and renal blood flow increased. This suggests a dopamine mediated renal vasodilation and natriueresis. Haloperidol and pimozide, both dopamine blocking agents with minimal blocking effects, prevented the natriuretic response. It was concluded that propranolol may increase sodium excretion directly by blocking beta receptors in the distal nephron and indirectly by dopamine mediated renal vasodilation. 26 references. (Author abstract modified)

002219 Chiel, Hillel J.; Wurtman, Richard J. Laboratory of Neuroendocrine Regulation, Massachusetts Institute of Technology, Cambridge, MA 02139 **Suppression of amphetamine-induced hypothermia by the neutral amino acid valine.** Psychopharmacology Communications. 2(3):207-217, 1976.

The effects of the neutral amino acid valine on amphetamine induced hypothermia were investigated. Pretreatment with valine (0.5to 2.0mmoles/kg) can suppress the hypothermic response of rats placed in a 4 degree C environment and given d-amphetamine sulfate. The amino acid was most effective when given 30 minutes before amphetamine administration, at which time it also significantly lowered brain tyrosine concentration (and, presumably, suppressed catecholamine synthesis). Because dopaminergic neurons mediate the hypothermic response to amphetamine and because amphetamine's ability to produce hypothermia requires, in part, the release of newly synthesized dopamine, these observed effects of valine pretreatment support the hypothesis that treatments which alter precursor (tyrosine) availability also affect brain catecholamine synthesis. 15 references. (Author abstract)

002220 Chugunov, V. V. Laboratoriya psikhofarmakologii NII po biologicheskim ispytaniyam khimicheskikh soyedineniy, Moscow, USSR /**Action of antidepressants on convulsive effect of corazol and strychnine.**/ Vliyaniye antidepressantov na sudorozhnoye deystviye korazola i strikhnina. Farmakologiya i Toksikologiya (Moskva). 39(6):658-662, 1976.

The effects of 10 antidepressants on experimentally induced convulsive syndrome were studied in mice. Results showed that antidepressants with sedative action, or melipramine, amitryptiline, chlorprothixen and phthoracizine protected against corazol convulsion; antidepressants with stimulating action, or iproniazide, nuredal, phrenolon and insidon potentiated the corazol effect; sonapax and desipramine had no substantial effect on corazol action. 14 references. (Journal abstract modified)

002221 Chung, Ho; Brown, David R. Department of Pharmacology and Toxicology, U. of Maryland School of Pharmacy, Baltimore, MD 21201 **The mechanism of the effect of acute stress on hexobarbital metabolism.** Toxicology and Applied Pharmacology. 37(2):313-318, 1976.

The effect of acute stress (unilateral hind leg ligation for 1 hr) on hepatic metabolism of hexobarbital (HB) was studied in the rat. A stress duration/response relationship was found for stress inhibition of HB metabolism. The hepatic microsomal protein content was not affected, but the hepatic microsomal cytochrome P-450 content was reduced approximately 45% by this stress treatment. Physical stress caused a twofold increase in plasma corticosterone level and had no effect on plasma corticosterone level of adrenalectomized rats. Hexobarbital metabolism was not affected by physical stress in adrenalectomized rats. Thus, the inhibition of hepatic HB metabolism by acute stress may be caused by the increased release of corticosterone induced by acute stress. 13 references. (Author abstract)

002222 Clamage, Dena M.; Sanford, Christy S.; Vander, Arthur J.; Mouw, David R. Department of Physiology, University of Michigan, Ann Arbor, MI 48109 **Effects of psychosocial stimuli on plasma renin activity in rats.** American Journal of Physiology. 231(4):1290-1294, 1976.

The effects of two types of psychosocial stimuli on plasma renin activity (PRA) were studied in unanesthetized rats. Blood was collected by decapitation. Thirty minutes of exposure to a novel environment ("open field") produced statisti-

cally significant increases of PRA in rats maintained on either a standard or sodium free diet. No change in plasma renin substrate occurred. Prior treatment with propranolol reduced the renin response by approximately 50% but did not completely abolish it. Plasma renin activity was also increased significantly by exposure of caged rats to the presence of a hungry cat for 30 min. It is concluded that psychosocial stimuli can produce significant increases in renin secretion and that this response is mediated, at least in part, by the sympathetic nervous system. 33 references. (Author abstract)

002223 Coelle, E. -F.; Osborne, N. N.; Neuhoff, V.; Sontag, K. -H. Max-Planck-Institut fur Experimentelle Medizin, Hermann-Rein-Strasse 3, D-3400 Gottingen, Germany **Failure of benzoctamine to influence the activity of rat striatum tyrosine-hydroxylase.** Arzneimittel-Forschung (Aulendorf). 26(8):1630-1631, 1976.

The effect of benzoctamine, a new minor tranquilizer, on striatum tyrosine hydroxylase activity was studied in albino rats 70-90 days old. Rats were injected i.p. with either saline, benzoctamine or alpha-methyl-p-tyrosine. After 2 to 3 hours, rats were decapitated and the striatum analyzed for tyrosine hydroxylase by its ability to convert C14-tyrosine to C14-dopa. Benzoctamine had no effect on tyrosine-hydroxylase activity, while alpha-methyl-p-tyrosine drastically inhibited tyrosine-hydroxylase activity. 9 references.

002224 Cohen, D.; Weinstock, M. Sackler School of Medicine, Tel Aviv, Israel **Evidence in favor of an anticholinergic mechanism of action of tricyclic antidepressant drugs.** Israel Journal of Medical Sciences (Jerusalem). 12(12):1516-1517, 1976.

A paper presented at the 35th meeting of the Israel Physiological and Pharmacological Society on evidence in favor of an anticholinergic mechanism of action of tricyclic antidepressant drugs is summarized. The direct antimuscarinic activity of five clinically equipotent tricyclic antidepressants: imipramine, chloriipramine, desipramine, iprindole and viloxazine, is reported. It was found that all five antidepressant drugs blocked the effect of a muscarinic agonist, MCN-A-343, in a dose range of 2 to 10 micragrams per cat. On the other hand, it was found that marked differences appeared in the amounts of these drugs required to potentiate noradrenaline.

002225 Collier, H. O. J.; Francis, D. L.; Roy, A. C. Miles Laboratories Ltd., Stoke Poges, Slough, SL2 4LY, England **Opiates, cyclic nucleotides, and xanthines.** Advances in Biochemical Psychopharmacology. 15:337-345, 1976.

Studies of the interaction of opiates with cyclic nucleotide mechanisms and with substances, such as E prostaglandins (PGEs) and xanthines, known to interact with these mechanisms are reviewed. In rat brain homogenate, opiates exert a dose related inhibition of PGE stimulated cyclic adenosine monophosphate (cAMP) formation. This effect is stereospecific and is correlated with agonist potency. Naloxone antagonizes heroin in a dose related way, without itself inhibiting PGE stimulated cAMP formation. In morphine dependent rats, intracerebroventricular injection of cAMP intensifies precipitated abstinence effects. Injection of dibutyryl cyclic guanosine monophosphate (dibutyryl cGMP) diminishes precipitated abstinence effects. In naive rats, the xanthines theophylline and 3-isobutyl-1-methylxanthine produce a quasimorphine abstinence syndrome that is readily suppressed by heroin and intensified by naloxone. In rat brain homogenate, these xanthines inhibit cyclic AMP phosphodiesterase. The findings are consistent with the views that: 1) opiates specifically inhibit an adenylate cyclase of morphine sensitive neurons that is sensitive to stimulation by PGEs; 2) opiate agonist action is associated with the lowering of a neuronal cAMP; 3) both the morphine abstinence syndrome in dependent rats and the quasiabstinence syndrome in naive rats are associated with a rise in neuronal cAMP; and 4) there are two types of endogenous humoral mediator acting on morphine sensitive neurons, one of which is morphinelike and the other antimorphinelike in action. 35 references. (Author abstract modified)

002226 Costa, E.; Cheney, D. L. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Regulation of cholinergic neurons by dopaminergic terminals: influence of cataleptogenic and noncataleptogenic antipsychotics. (Unpublished paper).** Washington, DC, NIMH, 1976. 25 p.

An overview of research into the effects of cataleptogenic and noncataleptogenic antipsychotics on the regulation of cholinergic neurons by dopaminergic terminals was presented during the Mario Negri Symposium. Various studies have shown that these antischizophrenic drugs can affect the turnover rate of acetylcholine (Ach) in the nuclei of rat brain. Single doses of haloperidol and chlorpromazine increase the turnover rate in the striatum and nucleus accumbens and decrease the rate in globus pallidus and hippocampus, and single doses of clozapine decrease the rate of turnover in globus pallidus. Repetition of dosages twice daily for 7 days ceases to result in a change in turnover rate of Ach in the striatum, nucleus accumbens and globus pallidus. Only the turnover rate of hippocampus continues to decrease after chronic haloperidol administration. The anticholinergic action does not develop tolerance whereas the blockage of dopamine (DA) dependent adenylate cyclase does. It is suggested that the antipsychotic action which does not develop tolerance may not derive from the blockade of its activation of adenylate cyclase by DA. 46 references.

002227 Costa, E.; Gnegy, M. E.; Uzunov, P. Laboratory for Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **Regulation of DA receptor sensitivity by an endogenous protein activator of adenylate cyclase. (Unpublished paper).** Washington, DC, NIMH, 1976. 5 p.

A series of investigations into the regulation of dopamine (DA) receptor sensitivity by an endogenous protein activator of adenylate cyclase in rats were briefly summarized in a report presented to the German and Polish Pharmacological Meeting in Hanover, Germany. Male rats were injected with haloperidol, clozapine, or butaclamol for 20 days. Behavioral responsiveness to apomorphine was evaluated 2 weeks after treatment and it was found that haloperidol and (+)-butaclamcol caused supersensitivity to apomorphine while clozapine and (-)-butaclamol did not. An increase in endogenous activator in the striatum of rats administered haloperdiol and (+)-butaclamol was found while no change was found in the clozapine and (-)-butaclamol groups. Adenylate cyclase activity was measured in the absence and presence of DA and it was found that when endogenous activator content was increased there was greater adenylate cyclase activity regardless of DA presence or absence. Data suggest that measurement of activator content in postsynaptic membranes of DA pathways may have some predictive value in determining chronic drug treatment potentials for causing tardive dyskinesia. 19 references.

002228 Curtis, D. R.; Lodge, D.; Johnston, G. A. R.; Brand, S. J. Department of Pharmacology, John Curtin School of

Medical Research, Canberra City, ACT 2601, Australia **Central actions of benzodiazepines.** Brain Research (Amsterdam). 118(2):344-347, 1976.

In an attempt to resolve conflicting reports concerning the interaction of benzodiazepines with receptors for the inhibitory transmitters glycine and gamma-aminobutyric acid (GABA) on mammalian central neurons, the effects of intravenous diazepam on the firing rates of individual Purkinje cells in the cerebellar vermis of anesthetized cats were studied. The firing rates of the cells were maintained at constant rates by electrophoretic application of DL-homocysteate. Diazepam produced no consistent changes in firing rate or in sensitivity to the DL-homocysteate. Neither the effect of electrophoretic GABA nor the duration of the synaptic duration of the evoked Purkinje cell was reduced. Further experiments found no reduction in the inhibitory effects of GABA or glycine. It is suggested that benzodiazepines neither mimic nor antagonize the action of GABA or glycine on the spinal and cerebellar neurones of cats and that the action of benzodiazepines may be largely presynaptic, modifying the release of GABA from terminals. 23 references.

002229 Davies, J.; Dray, A. Department of Pharmacology, School of Pharmacy, 29/39 Brunswick Square, London WC1N 1AX, England **Actions of enkephalin and morphine on spinal cord and brain stem neurones.** British Journal of Pharmacology (London). 58(3):458P-459-, 1976.

In a paper presented at a meeting of the British and French Pharmacological Societies, Sept. 1976, at Oxford, England, the actions of enkephalin and morphine on spinal cord and brainstem neurons in the cat and rat were studied. In the spinal cord, morphine and enkephalin caused excitation of Renshaw cells but not other noncholinoceptive interneurons. Both morphine and enkephalin induced excitation were reversibly reduced by naloxone. Neither drug depressed the firing rate of any spinal neurons. The effects on brainstem neurons were qualitatively similar. These results provide evidence for the hypothesis that enkephalin acts on central opiate receptors and is probably the endogenous ligand for the stereospecific opiate receptor. 5 references.

002230 de Repentigny, L.; Hanasono, G. K.; Plaa, G. L. Department of Pharmacology, Faculty of Medicine, University of Montreal, Montreal, Quebec H3C 3T7, Canada **The influence of acute diazepam pretreatment on the action and disposition of (14C)pentobarbital in rats.** Canadian Journal of Physiology and Pharmacology (Ottawa). 54(5):671-674, 1976.

The question of whether acute diazepam (DZP) pretreatment lengthens pentobarbital induced narcosis in rats by altering the disposition of pentobarbital in the body or by enhancing the sensitivity of the brain to this barbiturate was investigated. DZP pretreatment of rats 6 hours before pentobarbital administration prolonged the barbiturate induced narcosis. The concentrations of (14C)pentobarbital and total pentobarbital derivatives in blood or brain showed no differences between control and DZP pretreated animals. The brain and blood concentrations of pentobarbital, when measured at a time corresponding to the respective arousal times from pentobarbital narcosis, were lower in the DZP pretreated group. These results indicate that acute DZP pretreatment increases the sensitivity of the rat brain to pentobarbital rather than inducing changes in the dispositon of the barbiturate. 10 references. (Author abstract modified)

002231 Del Rio, Joaquin; Madronal, Javier. Institute of Medicinal Chemistry, CSIC, Juan de la Cierva 3, Madrid 6, Spain **Effect of neuroleptics and of combinations of d-amphetamine and neuroleptics on 3H-dopamine uptake by homogenates from rat striatum.** European Journal of Pharmacology (Amsterdam). 39(2):267-274, 1976.

The effect of neuroleptics and of combinations of d-amphetamine and neuroleptics on 3H-dopamine uptake by homogenates from rat striatum was studied. Triperidol was found to be a more potent 3H-dopamine uptake inhibitor than chlorpromazine in homogenates from rat striatum. Inhibition kinetics were competitive for triperidol and noncompetitive for chlorpromazine. When drugs were given in vivo, d-amphetamine blocked the 3H-dopamine uptake by about 50% whereas the neuroleptics did not modify the process even at highly sedating doses. Triperidol potentiated the blocking effect of d-amphetamine on 3H-dopamine uptake. The results tend to suggest that the postulated actions of neuroleptics on presynaptic sites in the striatum may be more important with the butyrophenone, triperidol than with the phenothiazine, chlorpromazine. 27 references. (Author abstract modified)

002232 Dill, R. E.; Davis, W. L.; Thonnard-Phillips, I. Department of Microscopic Anatomy, Baylor College of Dentistry, 800 Hall St., Dallas, TX 75226 **Motor disturbances produced by intrastriatal injection of cyclic AMP and cyclic GMP.** Archives Internationales de Pharmacodynamie et de Therapie (Ghent). 224(1):133-144, 1976.

Male albino rats were permanently cannulated bilaterally in the caudate/putamen nucleus and subsequently injected unilaterally with adenosine 3′,5′-monophosphate (cyclic AMP) or quanosine 3′,5′-monophosphate (cyclic GMP). Both of these cyclic nucleotides failed to produce any obvious change in motor activity. The concomitant intrastriatal injection of carbachol and cyclic AMP resulted in enhancement of the carbachol induced dyskinesias. Under similar conditions, cyclic GMP blocked the carbachol effects. The dibutyryl (db) derivates of cyclic AMP and cyclic GMP both enhanced the carbachol induced dyskinesias and both db cyclic nucleotides induced dyskinesias when injected intrastriatally alone. The concomitant intrastriatal injection of dopamine and carbachol resulted in a blockade of the carbachol induced dyskinesias. Dopamine had no effect on db cyclic AMP and db cyclic GMP dyskinesias. The db cyclic AMP effects characteristically involved the distal limb musculature, while the db cyclic GMP effects largely involved the proximal limb and trunk muscles. The hypothesis for opposing action of cyclic AMP and cyclic GMP in the CNS and the discrepancy between the effects of intrastriatal injection of cyclic AMP and dopamine were discussed. 36 references. (Author abstract)

002233 Doller, Herbert John, Jr. Pennsylvania State University, University Park, PA 16802 **L-dopa: plasma pharmacokinetics and conversion to dopamine in brain. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-29628 HC$15.00 MF$8.50 194 p.

The plasma pharmacokinetics of L-dopa in the presence and absence of a dopa-decarboxylase inhibitor (Ro-4-4602) and the relationship between plasma L-dopa concentrations and dopamine (DA) concentrations in various brain regions were studied in rabbits. Data analyses revealed that while exogenously administered L-dopa is decarboxylated to DA in monoaminergic terminals throughout the brain, elevated levels are not maintained in rabbit brain. DA concentrations of a region, including the striatum, rapidly follow fluctuations in plasma L-dopa concentrations. Kinetic reinterpretation of published clinical data from Parkinsonian patients treated with L-dopa supported this finding. Short-term beneficial effects or

central side-effects could be directly proportional to the rise and fall of DA in the brain, while long-term actions may not be proportional to elevated DA concentrations and may be related to changes in other parameters, such as RNA concentrations, glutamic acid dehydrogenase activity, relative lipid concentrations, or carbohydrate metabolism. (Journal abstract modified)

002234 Donaldson, Ivan McG.; Dolphin, Annette; Jenner, Peter; Marsden, Charles D.; Pycock, Christopher. University Department of Neurology, Denmark Hill, London SE5, England **The roles of noradrenaline and dopamine in contraversive circling behaviour seen after unilateral electrolytic lesions of the locus coeruleus.** European Journal of Pharmacology (Amsterdam). 39(2):179-191, 1976.

The roles of noradrenaline and dopamine in contraversive circling behavior seen after unilateral electrolytic lesions of the locus coeruleus were studied to determine the mechanism of action. One week after lesioning, apomorphine and d-amphetamine elicit contraversive circling behavior, which was not affected by noradrenergic receptor blockade but was abolished by dopamine receptor blockade. The drug induced contraversive circling response was reproduced by piribedil but not clonidine. Combined unilateral electrolytic locus coeruleus and substantia nigra lesions on the same side resulted in apomorphine and d-amphetamine induced ipsilateral rotational behavior. The results suggest that the circling behavior seen after unilateral locus coeruleus lesions depends on an asymmetry of striatal dopamine receptor activity and are consistent with a proposed coeruleus nigral noradrenergic pathway, which enhances impluse flow in the dopaminergic nigrostriatal system. 35

002235 Dutov, A. A. Chitinskiy meditsinskiy institut, Chita, USSR **/Effect of catecholaminergic agents on the circular reaction induced by stimulation of the caudate nucleus./** Vliyaniye katekholaminergicheskikh veshchestv na tsirkulyarnuyu reaktsiyu, vyzvannuyu razdrazheniyem khvostatogo yadra. Farmakologiya i Toksikologiya (Moskva). 39(5):537-540, 1976.

The effect of substances which strengthen central monoaminergic transmission and those which depress it, on the circular reaction induced by stimulation of the caudate nucleus was studied in 144 tests on 26 cats. The criteria used were contralateral turns of the head or running in circles. L-DOPA and apomorphine depressed the circular reaction, while aminazine (chlorpromazine) and haloperidol facilitated the effect. L-DOPA and aminazine had more pronounced effect on the reaction than apomorphine and haloperidol. It is suggested that dopaminergic and noradrenergic systems of the brain participate in mechanisms of the circular reaction. 6 references. (Author abstract modified)

002236 Erickson, Carlton K. Department of Pharmacology and Toxicology, School of Pharmacy, University of Kansas, Lawrence, KS 66045 **Regional distribution of ethanol in rat brain.** Life Sciences (Oxford). 19(9):1439-1446, 1976.

The cerebral distribution of a low i.p. dose of ethanol (ETOH) was studied using a double barrelled, membrane tipped perfusion cannula in rats to determine whether there is a differential distribution of ETOH in specific brain areas. Peak levels were reached earliest in the lateral ventricle and reticular formation. In a related study, homogenized (whole) brain ETOH levels were found to be similar to blood levels while flushed (bloodless) brain ETOH levels were approximately 20% lower than those found in blood and whole brain. It is concluded that there is a significant differential distribution of ETOH in the rat brain after a low dose of ETOH, and that this unequal brain ETOH distribution may influence the behavioral effects of the drug. 18 references. (Author abstract modified)

002237 Ferrendelli, James A. Departments of Pharmacology and Neurology, Washington University School of Medicine, St. Louis, MO 63110 **Cellular depolarization and cyclic nucleotide content in central nervous system.** Advances in Biochemical Psychopharmacology. 15:303-313, 1976.

Studies of the effects of depolarizing agents on cyclic nucleotide levels in brain regions from several mammalian species and studies of mouse cerebellum attempting to define the mechanisms by which cellular depolarization affects cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP) levels in this tissue are summarized. Several substances that cause cellular depolarization in excitable tissues, including veratridine, batrachotoxin, ouabain, and high levels of potassium ion, produce elevations of cAMP and cGMP. The effect of high potassium ion concentration on cyclic nucleotide levels varies quantitatively with respect to brain region and animal species. Evidence indicates that cellular depolarization leads to elevation of cAMP and cGMP levels by two different and unrelated mechanisms. cAMP levels appear to be elevated at least partly via a cellular depolarization induced release of adenosine in the CNS. Other factors which may contribute to the elevation of cAMP after cellular depolarization have not been identified. It appears that the influx of calcium ion into intracellular spaces produced by cellular depolarization (rather than cellular depolarization per se) results in increased levels of cGMP. The specific effects of calcium ion, magnesium ion, and other divalent cations on the cGMP response suggest a close relationship between the cyclic nucleotide and a process associated with release of one or more as yet undefined neurotransmitters. Whether this involvement occurs in presynaptic mechanisms or postsynaptic mechanisms also remains to be determined. 16 references.

002238 Fischer, J. F.; Cho, A. K. Department of Pharmacology, University of California School of Medicine, Los Angeles, CA 90024 **Properties of dopamine efflux from rat striatal tissue caused by amphetamine and p-hydroxyamphetamine.** Proceedings of the Western Pharmacological Society. 19:179-182, 1976.

Properties of dopamine efflux from rat striatal tissue caused by amphetamine (Amp) and p-hydroxyamphetamine (pOHA) are described in a preliminary report of a study examining the relationship between accumulation of sympathomimetic amine and release of neurotransmitter. Rat striatal tissue homogenates were preloaded with 3H-dopamine (3H-DA) and the ability of d-Amp and pOHA to release the 3H-DA was studied. Results indicate that while pOHA and d-Amp are equipotent as releasing agents, pOHA is accumulated 40 times more than d-Amp. 10 references. (Author abstract modified)

002239 Fluckiger, E.; Marko, M.; Doepfner, W.; Niederer, W. Sandoz Ltd., Biological and Medical Research Division, CH-4002, Basel, Switzerland **Effects of ergot alkaloids on the hypothalamic-pituitary axis.** Postgraduate Medical Journal (Oxford). 52(Supplement 1):57-61, 1976.

In a paper presented at a symposium on ergot compounds in London in May 1975, the effects of ergot alkaloids on the hypothalamic/pituitary axis were reported. Using implantation inhibition in rats to study the natural peptide derivatives of lysergic acid, great differences in potency were seen between the different representatives of this group of drugs. Maximal

activity was found with the components of ergotoxine and the rating potencies of those alkaloids showed that the potency of ergokryptine was greater than that of ergocornine which was greater than that of ergovaline. A comparison of vascoconstrictor potencies of 2-bromo-alpha-ergokryptine (CB 154) and the standard compound ergotamine in spinal cat preparation showed that CB 154 had less than 0.5% the activity of the standard. On the basis of studies reported, it is seen that CB 154 shows a high specificity of action for the prolactin system but that an endocrine derangement exists where the primary action of CB 154 is accompanied by a facilitation of gonadotrophin secretion and another endocrine derangement where CB 154 attenuates the secretion of GH. CB 154 acts at two sites, the pituitary and the CNS, and at both sites the same mechanism of action, stimulation of DA-receptors, is exerted. 38 references. (Author abstract modified)

002240 Frigerio, A.; Pantarotto, C. Instituto di Richerche Farmacologiche "Mario Negri" Via Eritrea 62, I-20157 Milan, Italy **Epoxide-diol pathway in the metabolism of tricyclic drugs.** Journal of Pharmacy and Pharmacology (London). 28(8):665-666, 1976.

In a letter to the editor, the metabolism of the tricyclic antidepressants opipramol and intriptyline, and the anticonvulsant cytenamide as studied in vivo in rats and in vitro with rat liver microsomes, along with two model compounds, is reported. The major sequences of biotransformation in these tricyclic drugs were by epoxidation of the 10,11-double bond. The epoxides proved to be relatively stable and not cytotoxic to cell cultures. A tentative biochemical structure for arene oxide metabolites of these tricyclics are presented, and offered as a possible explanation for the toxic side-effects of several other tricyclic drugs. 7 references.

002241 Fujieda, Toshiyoshi; Ueno, Takeharu; Yamashita, Kaku. Department of Neuropsychiatry, Hokkaido University, Hokkaido, Japan **Changes in the amine and adrenal cortical hormone levels within the brains of rats after administration of disulfiram.** Psychiatria et Neurologia Japonica (Tokyo). 78(8):578, 1976.

In a paper read at the 48th Hokkaido Psychoneurolgical Smyposium held in December 1975 at Sapporo, Japan, the effects of acute and chronic administration of disulfiram to rats on amine and adrenal cortical hormone levels in the blood serum was measured over a 24 hour period. After acute administration of disulfiram spontaneous activity of the rats decreased; after chronic administration the pattern of rest in the daytime and activity during nighttime was preserved, but activity was reduced, reflected in changes of the quantities of the adrenal cortical hormone levels. With acute administration, levels would rise after two hours; with chronic administration levels would be highest at 9 p.m. and lowest at 9 a.m. Levels would also drop off when the rats rested at night.

002242 Fuller, Ray W.; Perry, Kenneth W.; Baker, John C. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Duration of the effects of alpha-ethyl-4-methyl-m-tyramine, (H75/12) on brain 5-hydroxyindole concentrations in rats.** Journal of Pharmacy and Pharmacology (London). 28(8):649-650, 1976.

The duration of action of the amphetamine derivative alpha-ethyl-4-methyl-m-tyramine (H75/12), changes in 5-hydroxyindoleacetic acid (5-HIAA) brain concentrations after H75/12 administration, and the possibility that H75/12 may lead to reduced tryptophan hydroxylase activity are investigated in the rat. Whole brains of rats decapitated after injection with H75/12 were spectrofluorometrically examined. Results indicated that after H75/12 administration the duration of 5-hydroxytryptamine (5-HT) is very short compared with that produced by 4-chloroamphetamine, despite the fact that, like 4-chloroamphetamine, H75/12 is apparently a substrate for the amine pump on the neuronal membrane. It is suggested that the ability to be taken into the neuron by the amine pump is not sufficient to account for the long duration of action of 4-chloroamphetamine. 10 references.

002243 Fuller, Ray W.; Perry, Kenneth W.; Clemens, James A. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Elevation of 3,4-dihydroxyphenylacetic acid concentrations in rat brain and stimulation of prolactin secretion by fenfluramine: evidence for antagonism at dopamine receptor sites.** Journal of Pharmacy and Pharmacology (London). 28(8):643-644, 1976.

To test the blocking effect of fenfluramine on dopamine receptors, concentrations of 3,4-dihydroxyphenylacetic acid (DOPAC), an intraneuronal metabolite of dopamine, was measured in the rat brain. The effects of fenfluramine and norfenfluramine on prolactin concentrations in rat serum were also measured. The findings that fenfluramine and norfenfluramine cause rapid increases in concentrations of brain DOPAC and serum prolactin support the hypothesis that fenfluramine can antagonize dopamine receptors. The action of fenfluramine appears to be more complex than that of simple dopamine receptor antagonists, since at later times it lowers DOPAC concentrations as do other amphetamines. 12 references. (Author abstract modified)

002244 Furukawa, Kiyoshi; Karasawa, Tadahiko; Ochi, Yoshiaki; Yoshida, Kouichi; Shimizu, Masanao. Research Laboratories, Dainippon Pharmaceutical Co. Suita, Osaka 564, Japan **Levels of brain O-methylated catecholamines as an index for the release of catecholamines by centrally acting drugs.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):105P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March 1976, a study of the levels of brain O-methylated catecholamines measured as an index for the release of catecholamines by centrally acting drugs in rats was reported. The changes in the levels of normetanephrine (NM) and 3-methoxytyramine (3-MT) induced by psychotropic drugs under monoamine oxidase inhibition produced by pargyline dosely paralleled the changes in the levels of brain 3-methoxy-4-hydroxyphenylethylene glycol sulfate (MOPEG) and homovanillic acid (HVA) induced by the same drugs with no monoamine oxidase inhibition. Cocaine, methamphetamine, haloperidol and chlorpromazine increased the levels of 3-MT, NM, HVA and MOPEG, though the extend of the increase was different among the drugs. Apomorphine decreased the levels of 3-MT and HVA but increased both NM and MOPEG levels. Clonidine decreased NM and MOPEG levels without affecting the levels of 3-MT and HVA. Phenoxybenzamine increased NM and MOPEG at high doses. Propranolol and diazepam had no significant effect on the level of any metabolite, though a tendency toward a decrease in 3-MT and HVA was observed with diazepam. (Author abstract modified)

002245 Furukawa, Tatsuo; Yamazaki, Michiyo; Hiraga, Yuko; Fukazawa, Eiko; Kushiku, Kazushi; Nakano, Ushio. Department of Pharmacology, School of Medicine, Fukuoka University, Fukuoka 814, Japan **Potentiation of effects of catecholamines and sympathetic stimulation by triazolobenzodiazepine.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):52P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study of the potentiation of effects of catecholamines and sympathetic stimulation by a triazolobenzodiazepine (triazolam) was reported. Triazolam did not elicit an analgesic effect in mice, but it tended to potentiate the analgesic effect of morphine and to inhibit the cough reflex in dogs. It induced a slight decrease in blood pressure and heartrate without noticeable changes in cardiac contractile force in dogs. After triazolam in dogs, cardiovascular responses to the carotid reflex and vagus stimulation were not affected, but those to preganglionic and postganglionic stimulation of the cardiac ganglion were potentiated. Cardiac responses to noradrenaline and adrenaline were potentiated. Triazolam slightly reduced heartrate without affecting the amplitude of movements and tended to potentiate the actions of catecholamines in isolated atrium preparation of guinea-pigs. The actions of acetylcholine, histamine, serotonin and barium on smooth muscle preparations were not affected. It is suggested that triazolam exhibits similar pharmacological actions but different relative potencies in each action when compared to other benzodiazepines, and that, when triazolam is administered in large doses, sympathetic functions are accelerated. (Author abstract modified)

002246 Gallager, Dorothy W.; Aghajanian, George K. Department of Psychiatry, Yale University School of Medicine, New Haven, CT 06508 **Effect of antipsychotic drugs on the firing of dorsal raphe cells. I. Role of adrenergic system.** European Journal of Pharmacology (Amsterdam). 39(2):341-355, 1976.

The affect of antipsychotic drugs on the firing of dorsal raphe cells in the brain was investigated. The activity of serotonergic (5HT) neurons in the dorsal raphe nucleus was inhibited by the i.v. administration of certain antipsychotic drugs (methiothepin, clozapine and thioridazine). Other antipsychotic agents did not inhibit raphe cell firing. An alpha-adrenergic blocking agent, piperoxane, but not the the beta-blocking agents, propranolol and MJ 1999, inhibited raphe activity when administered systemically. All of these drugs appear to act indirectly since they (and NE) have relatively weak or variable effects when applied microiontophoretically to raphe neurons. Data suggest that these drug effects may be mediated by an adrenergic pathway ascending from the lower brainstem. 78 references. (Author abstract modified)

002247 Gallager, Dorothy W.; Aghajanian, George K. Department of Psychiatry, Yale University School of Medicine, New Haven, CT 06508 **Effect of antipsychotic drugs on the firing of dorsal raphe cells. II. Reversal by picrotoxin.** European Journal of Pharmacology (Amsterdam). 39(2):357-364, 1976.

An examination of the effects of two inhibitory amino acid transmitters for possible effects on dorsal raphe cell firing using single cell recording and microiontophoretic techniques is presented. The ability of the GABA antagonist, picrotoxin and the glycine antagonist, strychnine, to reverse the effects of the antipsychotic and alpha-blocking drugs on dorsal raphe firing was tested. Both GABA and glycine were found to inhibit raphe cell firing selectively, allowing for a possible neurotransmitter function for these amino acids within the dorsal raphe nucleus. Picrotoxin but not strychnine was found to reverse the effects of the antipsychotic and alpha-blocking drugs on raphe firing. It is concluded that the adrenergic input may influence 5-HT neurons indirectly via a GABAergic interneuron or interposed GABA neuron. 31 references. (Author abstract modified)

002248 Gavlik, I.; Yanku, I.; Pochatov, Yu. M.; Rayevskiy, K. S. Institut farmakologii Chekhoslovatskoy akademii nauk, Prague, Czechoslovakia **/Pharmacokinetic study of the neuroleptic azabutyron./** Farmakokineticheskoye izucheniye neyroleptika azabutirona. Farmakologiya i Toksikologiya (Moskva). 39(4):402-406, 1976.

Dependence of pharmacological traits of azabutyron on features of its distribution and elimination from the body were studied in male rats and male rabbits using spectrophotometric analysis and chromatography. The effects of the drug were observed in the plasma, bile, gastric juice, and urine, using a two compartment pharmacokinetic model. The concentration of azabutyron in plasma achieved maximum percentage of the original dose five minutes after injection. The amount of unchanged drug excreted with the urine was 2% to 4% of the dose, and less than 1% was found in the bile and gastric juice. It is suggested that a two compartment model is insufficient to explain the pharmacokinetic traits of azabutyron, and a three compartment model, at least, is needed. 4 references.

002249 Gianutsos, Gerald; Lal, Harbans. Department of Pharmacology, School of Pharmacy, University of Rhode Island, Kingston, RI 02881 **Drug-induced aggression.** In: Essman, W., Current developments in psychopharmacology. New York, Spectrum, 1976. 393 p. v. 3. (p. 197-220).

Studies on aggression induced by drugs and on the role of various neurotransmitters in the mediation of drug induced aggression are reviewed. Dopamine (DA) receptor agonists, both directly and indirectly acting, produce aggression and potentiate morphine withdrawal induced aggression. Neuroleptics, which are thought to block DA receptors, reduce or block aggression induced by DA agonists such as apomorphine or by morphine withdrawal. It is suggested that DA plays a major role in the elicitation of aggressive behavior. Studies using parachlorophenylalanine (PCPA), an inhibitor of serotonin (5-HT) synthesis, and 5-hydroxytryptamine, a 5-HT precursor, suggest that 5-HT may have an inhibitory effect on drug induced aggression. It appears likely that this effect is mediated through an antagonism of the effects of DA stimulation. Investigations into the involvement of acetylcholine in aggression have produced equivocal results. Studies using the norepinephrine (NE) receptor agonist clonidine and alpha-adrenergic blockers and beta-adrenergic blockers have indicated enhancement, inhibition, or no effect on aggression, depending upon the experimental design and animal being studied. It is suggested that: 1) DA produces its effect on aggression by working in concert with other neurotransmitters; 2) NE may initiate or oppose DA activity in different anatomical sites; 3) normal 5-HT or acetylcholine activity may inhibit the expression of drug induced aggression; and 4) in nondopaminergic areas of the brain, 5-HT and ACh may be directly responsible for some of the emotional characteristisc or supportive behaviors associated with aggression. It is concluded that further experimentation is needed to prove or disprove these speculations. 112 references.

002250 Glisson, Silus N.; El-Etr, Adel A.; Bloor, B. C. Dept. of Anesthesiology, Loyola University Medical Center, 2160 South First Avenue, Maywood, IL 60153 **The effect of ketamine upon norepinephrine and dopamine levels in rabbit brain parts.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 295(2):149-152, 1976.

Ketamine was injected into adult male rats and adult male rabbits followed by excision and study of whole brain to investigate its effect on dopamine and norepinephrine levels. Ketamine significantly increased dopamine levels in the

thalamus and hypothalamus brain areas, but not in the midbrain or caudate nucleus. The increase in dopamine occurred during the time when ketamine produced its maximal anesthetic action (10 to 30 min). Ketamine had no effect upon norepinephrine levels in whole brain or the select brain parts with the exception of caudate nucleus at any of the times studied. It is suggested that these results demonstrate an effect of ketamine upon dopamine levels in those brain regions previously suggested as the site of ketamine's anesthetic action. 15 references. (Author abstract modified)

002251 Golovanova, I. V.; Gubanova, T. I.; Smirnova, Ye. I. Vsesoyuznyy NI khimiko-farmatsevticheskiy institut, Moscow, USSR **/Determination of the embryotoxic and teratogenic effects of the new antidepressant pyrasidol./** Opredeleniye embriotoksicheskogo teratogennogo deystviya novogo antidepressanta pirazidola. Farmakologiya i Toksikologiya (Moskva). 39(5):607-609, 1976.

An experiment to determine the embryotoxic and teratogenic traits of the new soviet antidepressant pyrasidol was performed, using massive injections in 409 pregnant white rats. The dose of 200mg/kg is 30 times that permissible for humans. An investigation of the ovaries of the mothers, number of dead fetuses and reabsorptions, and dimensions and skeletal defects of embryos was made, as well as of penetration of the placental membrane by the drug. A single injection had no effect. Study of the amniotic fluid of rats given the drug on the 15th and 20th days of pregnancy suggests direct contact of embryos with the metabolic products in the last trimester. 6 references.

002252 Gotoh, Yasuhito; Kobayashi, Masafumi; Sato, Mikio. Department of Pharmacology, Nihon University School of Dentistry, Tokyo 101, Japan **Role of brain noradrenaline on amphetamine-stereotypy -- effects of alpha-MPT, in particular.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):34P, 1976.

At the 49th meeting of the Japanese Pharmacological Society, Osaka, Japan in March, 1976, a study of the role of noradrenaline (NA) and serotonin (5-hydroxytryptamine, 5-HT) in amphetamine stereotypy was reported. Methamphetamine was administered to rats pretreated with alpha-methyl-paratyrosine (alpha-MPT) alone or in combination with safrazine or L-DOPA. Stereotyped behavior and brain levels of NA and 5-HT were measured at various intervals after injection. Methamphetamine stereotypies were depressed by alpha-MPT but were reversed by safrazine or L-DOPA. However brain NA depletion was not antagonized by either safrazine or L-DOPA. Brain 5-HT increases in safarzine treated rats were not antagonized by alpha-MPT. It is suggested that 5-HT may be involved in methamphetamine stereotypies. (Author abstract modified)

002253 Greenberg, David A.; Snyder, Solomon H. Department of Pharmacology, Johns Hopkins University School of Medicine, Baltimore, MD 21205 **Pharmacologic properties of (3H)dihydroergokryptine binding sites associated with alpha-noradrenergic receptors in rat brain membranes.** Research Report, NIMH Grant MH-18501, 1976. 29 p.

Research on the binding of (3H)dihydroergokryptine, or (3H)HDE, associated with alpha noradrenergic receptors in rat cerebral cortical membranes is reported, emphasizing that the compound is a mixed agonist/antagonist at these receptors and binds in a saturable fashion and with high affinity to cortex membranes. The regional distribution of binding in rat brain coincides with that observed for an alpha receptor binding of (3H)clonidine and (3H)WB-4101 except for disproportionately high levels in corpus striatum, suggesting that in striatal membranes (3H)HDE can also bind to dopamine. Hill coefficients for inhibition of (3H)HDE by mixed agonist/antagonists and by pure agonists or antagonists are consistent with a model of the alpha noradrenergic receptor in which agonists and antagonists bind selectively to discrete noninterconverting sites, while mixed agonist/antagonists can bind to either site. Overall findings are consistent with the existence of discrete agonist and antagonist states of alpha noradrenergic receptors. Ergot alkaloids are the most potent inhibitors of (3H)DHE binding. 29 references. (Author abstract modified)

002254 Grobecker, H.; Saavedra, J. M. McCarty, R.; Chiueh, C. C.; Kopin, I. J. Department of Pharmacolgy, University of Frankfurt, Frankfurt, Germany **Dopamine beta-hydroxylase activity and catecholamine concentrations in plasma: experimental and essential hypertension. (Unpublished paper)** Rockville, MD, NIMH, 1976.

Plasma dopamine beta-hydroxylase (DBH) activity, norepinephrine (NE) levels and epinephrine (E) levels were measured in blood samples obtained from 4-week-old spontaneously hypertensive rats (SHR), normotensive rats, and rats with experimentally induced hypertension. DBH activity and NE levels in plasma of SHRs were significantly elevated; however, in both SHRs and rats with experimentally induced hypertension, circulating DBH activity and NE levels were lower in plasma from blood samples obtained by arterial catheter than in blood samples obtained after decapitation. The effects of various treatments on plasma DBH activity and circulating catecholamine (CA) levels in normal human subjects and in hypertensive patients were also determined. In normotensive subjects, tyramine infusion increased circulating CA levels. However, after physical exercise both DBH activity and CA levels were increased. In hypertensive patients, no changes in resting NE and E plasma levels or DBH activity were observed before or after acute or chronic administration of propranolol. However, during propranolol treatment, exercise significantly increased circulating NE.

002255 Guidotti, A. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC **Methods to evaluate in vivo the activity of GABA receptor agonists. (Unpublished paper).** Washington, DC, NIMH, 1976. 19 p.

A series of studies with rats undertaken to develop methods for the estimation of gamma-aminobutyric acid (GAB) receptor activation utilizing muscimol, a model molecule for GABA receptor agonism, were discussed in a paper presented to the 10 Congress of the Collegium Internationale Neuropsychopharmacologicum held in Canada. By measuring the changes in concentration of 3',5'-cyclic adenosine monophosphate (cAMP) on A. pituitary or 3',5'-cyclic guanosine monophosphate (cGMP) in cerebellum of rats injected either locally or parenterally with muscimol it was possible to estimate in vivo the action of GABA receptor activation. It was found that: 1) GABA receptor agonists selectively antagonize convulsions produced by GABE receptor antagonists but not those produced by glycine receptor antagonists 2) cerebellar cGMP content is reduced by GABE receptor agonists injected locally in cerebellu, and systemic administration of GABA receptor agonists blocks the increase of cerebellar cGMP inducted by blockers of GABA receptor function; and 3) increase of A. pituitary cAMP induced by isoniazid and picrotoxin is blocked by muscimol while increase induced by reserpine is not. Pargyline, an MAO inhibitor, blocks effects of reserpine but not of isoniazid. 25 references.

002256 Guidotti, A.; Biggio, G.; Costa, E. Laboratory of Preclinical Pharmacology, National Institute of Mental Health, Saint Elizabeths Hospital, Washington, DC 20032 **Action of diazepam, haloperidol, morphine and muscimol on the cGMP content of cerebellum. (Unpublished paper).** Washington, DC, NIMH, 1976. 20 p.

Measurement of the effects of psychoactive drugs on the cyclic GMP (cGMP) content of the cerebellum is proposed as a model for determining whether a drug can be classified as a potential gamma-aminobutyric acid (GABA) agonist or a GABA antagonist. Investigations performed in rats revealed that: 1) muscimol and diazepam lower cerebellar cGMP when injected systemically or into the cerebellum but not when injected into the striatum; 2) haloperidol and morphine reduce cerebellar cGMP when injected into the striatum but not when injected into the cerebellum; 3) the effect of haloperidol is specifically blocked by apomorphine; 4) the effect of morphine is specifically blocked by naltrexone; and 5) the increase of cerebellar cGMP induced by intracerebellar isoniazid is blocked only by diazepam and muscimol. It is concluded that muscimol, diazepam, haloperidol and morphine decrease cerebellar cGMP content through different mechanisms. It is suggested that the similarity between the effects of diazepam and muscimol, a specific GABA agonist, supports the hypothesis that diazepam activates GABA receptors. 27 references.

002257 Hamlet, Martha Anne. University of California, San Francisco, CA **The role of central noradrenergic neurons in the control of pituitary-adrenocortical function in the rat. Effects of 6-hydroxydopamine and various sympathomimetic agents. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-17366 HC$15.00 MF$8.50 159 p.

To investigate the role of central noradrenergic neurons in the control of pituitary/adrenocortical function in the rat, the effects of chronic loss of these neurons by administration of the neurotoxic drug, 6-hydroxydopamine (6-OHDA) on adrenocorticotrophin (ACTH) secretion in adaptive situations were assessed. Various parameters of pituitary/adrenal function were examined in adult male Ss which had been subjected to long-term central norepinephrine depletion by third ventricular administration of 6-OHDA. These parameters included response to ether stress, suppressibility of stress induced corticoid secretion by dexamethasone, and response to bilateral and unilateral adrenalectomy. The question of why chronic hypersecretion of ACTH does not occur after long-term depletion of central norepinephrine was also investigated. Findings indicated that: 1) rats subjected to long-term central norepinephrine depletion are more sensitive to the feedback action of glucocorticoids on corticotrophin releasing factor (CRF)-ACTH secretion; 2) 6-PHDA treated rats did not exhibit compensatory adrenal hypertrophy 72 hr after unilateral adrenalectomy, but had significantly larger adrenals at the time of operation and unlike nondepleted controls, experienced no further growth of the remaining adrenal; 3) norepinephrine administration into the third ventricle in doses ranging from 0.1to 200 micrograms had no inhibitory effect on plasma corticoid response to a surgical stress and the stress response was not inhibited by central alpha-receptor stimulation with clonidine, a pure alpha agonist; and 4) acute effects of intraventricular 5-OHDA on resting plasma corticosterone levels revealed differences which were dependent on whether on not the drug was given with or without anesthetic. It is concluded that central noradrenergic neurons probably do not play a major role in controlling the tonic secretion of ACTH, but may be involved in the inhibitory feedback action of glucocorticoids on ACTH secretion. (Journal abstract modified)

002258 Han, Wesley W.; Yakatan, Gerald J.; Maness, Dale D. Searle Laboratories, Chicago, IL 60680. **Kinetics and mechanisms of hydrolysis of 1,4-benzodiazepines I: chlordiazepoxide and demoxepam.** Journal of Pharmaceutical Sciences. 65(8):1198-1204,1976.

The kinetics and mechanisms of hydrolysis of chlordiazepoxide and demoxepam over a wide pH range were evaluated by differential absorbance spectroscopy. Loss of the methylamino group from chlordiazepoxide produces demoxepam, which is degraded by a parallel consecutive reaction to 2-amino-5-chlorobenzophenone and a glycine derivative. Two intermediates occur during demoxepam hydrolysis. Amide hydrolysis appears to be the major reaction leading to the benzophenone product; splitting of the azomethine linkage probably represents an alternate but minor pathway. The stability parameters involving buffer catalysis, ionic strength effects, and temperature dependence of rate constants are reported. 8 references. (Author abstract modified)

002259 Hara, Toshio; Masuda, Kunio; Miyake, Hitoshi. Department of Neuropsychiatry, Kitasato University School of Medicine, Kanagawa, Japan **Effects of psychotropic drugs on the PGO waves occurring in REM sleep and on the reserpine-induced PGO waves.** In: Weitzman, E., Advances in sleep research. New York, Spectrum, 1976. 236 p. (p. 131-154).

Experiments were conducted on 23 adult cats with chronically implanted electrodes for EEG, EMG, and eye movements to determine the effects of psychotropic drugs on the ponto-geniculo-occipital waves (PGO waves) occurring in REM sleep and on reserpine induced PGO waves (PGO-res). Analysis of the direct action of various compounds on REM sleep and PGO waves indicated that chlorpromazine and haloperidol had no influences on all tonic and phasic events of REM sleep or on the PGO-res. Small doses of gamma-hydroxybutyrate (GHB) prolonged the REM sleep significantly. Marked dissociation of PGO waves from REMs was caused by pentobarbital and ketamine, benzodiazepines, and perphenazine caused only moderate dissociation. Benzodiazepines, ketamine, and GHB all preserved reappearance of REM sleep, alteration of PGO-res from isolated to burstlike, and decreased frequency of the hippocampal theta rhythm (HTR). Relatively small doses of L-DOPA had no influence on REM sleep, whereas higher doses, like methamphetamine, awakened Ss and eliminated PGO-res completely. Imipramine and amitriptyline markedly interrupted REM sleep and eliminated PGO-res, followed by synchronization of the neocortical EEG. Differences in susceptibility to psychotropic drugs between the REM sleep producing system, as well as the tonic event system, and the mechanism that generates the phasic events (particularly PGO waves) is discussed. The functional difference of isolated PGO-res from burstlike PGO waves is also suggested. 28 references. (Author abstract modified)

002260 Hornykiewicz, Oleh. Department of Psychopharmacology, Clarke Institute of Psychiatry, University of Toronto, Toronto, Canada **Neurohumoral interactions and basal ganglia function and dysfunction.** In: Yahr, M., The basal ganglia. Vol. 55. New York, Raven Press, 1976. 474 p. (p. 269-280).

In a paper presented at the 55th meeting of the Association for Research in Nervous and Mental Disease, clinical and experimental research on neurohumoral interactions and ganglia function and dysfunction was reviewed, suggesting that high concentrations of monoamines and related compounds (dopamine, acetylcholine, gamma-aminobutyric acid, serotonin, and norepinephrine) in these ganglia have been im-

plicated as putative central neurotransmitter substances, but that an alternate possibility must be considered. This option suggests that the principal role of the monoamines in the basal ganglia could be to regulate the level of system responsiveness in regard to rate and direction of neuronal impulse flow. The dense and fairly uniform innervation of the basal ganglia by chemically distinct systems suggests a high degree of convergence of the neurohumoral influences acting on the striatal neurons. It is proposed that this morphological/biochemical interrelation requires the existence of mechanisms coordinating the activity state of these multiple monoamine inputs, thus forming the basis for the neurohumoral interactions observed in the ganglia. The existence of complex neurohumoral interactions in the ganglia is supported by neuropharmacological and biochemical evidence obtained in laboratory animals and in basal ganglia disorders (Parkinson's disease and Huntington's chorea) in man. 33 references.

002261 Ikeda, Masahiro; Harada, Shigeko; Tsujimoto, Akira. Department of Pharmacology, Hiroshima University School of Dentistry, Hiroshima 734, Japan **Prevention of local anesthetic-induced convulsions by gamma-aminobutyric acid.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):44P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study of the participation of gamma-aminobutyric acid (GABA) in the induction of convulsions in rats was reported. Intraventricular GABA significantly prevented the induction of procaine induced convulsions in rats. Although GABA completely prevented convulsions induced by various local anesthetics (procaine; lidocaine; cocaine; tetracaine), the same dosage of GABA did not block convulsions produced by nicotine, pentylenetetrazol, strychnine, and picrotoxin. Tetracaine, cocaine and procaine slightly inhibited the spontaneous release and markedly inhibited the potassium stimulated release of GABA from rat brain synaptosomes preloaded with radiolabeled GABA. A slight inhibition of GABA uptake into synaptosomes by these local anesthetics was observed. Glutamic acid decarboxylase and GABA transaminase activities in rat brain were not influenced by these local anesthetics. The rat brain GABA level at the onset of local anesthetic convulsions was the same as the control level. It is suggested that inhibition of GABA release may be involved in the mechanism of production of convulsions induced by local anesthetics. (Author abstract modified)

002262 Ishii, Hiroshi; Fujisaki, Tadashi; Goto, Toshio; Ito, Yasukiyo; Kojima, Kikuo. Department of Pharmacology, Kagoshima University School of Medicine, Kagoshima 890, Japan **Experimental studies on intoxication or detoxication of methylmercuric chloride.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):85P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study of the effects of single and multiple doses of methylmercuric chloride (MMC) in rat brain was reported. Mercury (Hg) contents in the brain showed a correlation with the doses of intravenously injected MMC. The Hg contents were increased within 5 min after administration of MMC, but higher Hg levels in the brain observed 24 hr after administration. Norepinephrine (NA) and serotonin (5-HT) in the brain increased 3 hr to 24 hr after a single dose of MMC. With chronic administration of MMC, 5-HT contents in the brain showed a tendency to increase while those of NA decreased. Hg contents in the brain increased with electric stimulation given immediately after an intravenous injection of MMC. The Hg contents decreased with electric stimulation given 3 hr to 24 hr after the injection but changes in Hg contents in the brain 5 min after the intraventricular injection of MMC decreased with electrical stimulation. Reserpine, chlorpromazine, p-chlorophenylalanine and alphamethyl-p-tyrosine decreased Hg uptake in the brain. (Author abstract modified)

002263 Itoh, Tadao; Ichida, Seiji; Hata, Fumiaki; Yoshida, Hiroshi. Center for Adult Diseases, Osaka 537, Japan **Pharmacological studies on development of response to catecholamine in brain.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):162P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March 1976, a pharmacological study on the development of responses to catecholamines (CA) in infant rat brain was reported. The binding of CA with brain synaptic membrane fraction (SMF) was investigated using norepinephrine (NE) as the binding CA. The binding of NE was temperature dependent, and bound NE was partially released by the addition of a relatively high concentration of NE into the incubation medium. Ferrous ion enhanced the binding remarkably. Various catechol compounds inhibited the binding. Phentolamine and propranolol did not affect the binding. SMF prepared from infant (2-day-old) rat brain had a higher NE binding activity than that of adult brain. Both adult and infant adenylate cyclase activity in SMF was demonstrated in the presence of sodium fluoride. Cyclic adenosine monophosphate (cyclic AMP) content in adult rat brain cortex slices was increased by NE. In infant rat brain slices, the cyclic AMP content was significantly lower than in adult rat brain slices and NE response to the cyclic AMP was not observed. It is suggested that development of the CA response to the receptor adenylate cyclase/cyclic AMP system in infant brain may be due to the formation of SMF or an intracellular coupler connecting the receptor to the adenylate cyclase system. (Author abstract modified)

002264 Iwata, Heitaroh; Tsukamoto, Toshihiko; Baba, Akemichi; Matsuda, Toshio. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Osaka University, Osaka 565, Japan **Effect of chlorpromazine on cyclic AMP phosphodiesterase in rat cerebral cortex.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):109, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March 1976, a study of the effects of chlorpromazine (CPZ) on particulate cyclic adenosine monophosphate (AMP) phosphodiesterase (PDE) activity in crude synaptosomes from rat cerebral cortex was reported. Particulate PDE activity was activated by calcium ion (Ca) in the presence of a protein activator (PA), but not by Ca alone. CPZ inhibited Ca/PA activated PDE activity, but not the basal activity on the enzyme. The binding of Ca to the particulate fraction was also inhibited by CPZ. Enzyme activity was enhanced by Triton X-100 and phospholipase C treatment. The activity was also increased under alkaline pH conditions, and at alkaline pH the rate of CPZ inhibition increased. The findings suggest that the inhibitory effect of CPZ may be due to a change in Ca movement and that the particulate PDE activity is regulated by a protein/lipid structure in the membrane. (Author abstract modified)

002265 Iwatsubo, Katsuya. Department of Pharmacology, Osaka University Dental School, Osaka 530, Japan **Effect of morphine and haloperidol on single cell activity of nigrostriatal neurons.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):17P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study of the effects of morphine and haloperidol on single cell activity of nigrostriatral neurons of the rat was reported. Morphine increased the firing rate of substantia nigrazona compacta (SNC) cells. Haloporidol also produced an increase in firing rate. The increase in firing rate produced by morphine was diminished to the basal rate by levallorphan and naloxone, while the effect of haloperidol remained unchanged. Morphine also increased the firing rate of caudate neurons; this effect was also antagonized by naloxone and the dopamine receptor agonists apomorphine and DOPA. The sites of achon for the opiate and neuroleptic effects of these agents are discussed. (Author abstract modified)

002266 Jacobowitz, David M. Laboratory of Clinical Science, NIMH, Bldg 10/Rm 2D-46, Bethesda, MD 20014 **Histochemical and micropunch analysis of aminergic and cholinergic pathways. (Unpublished paper).** Bethesda, MD, NIMH, 1976. 17 p.

A summary of the localization of brain catecholaminergic and cholinergic axonal pathways and areas of terminal innervation based on histochemical and micropunch analyses of rat brain is presented. Noradrenergic and dopaminergic pathways are discussed and noradrenergic axonal pathways are plotted on transverse sections of a stereotaxic atlas. The dorsal and ventral pathways, two distinct major bundles, are described. Directions for future neuropsychopharmacological research are briefly reviewed. 35 references.

002267 Jacquet, Yasuko F.; Marks, Neville. New York State Research Institute for Neurochemistry, Rockland Psychiatric Institute, Ward's Island, New York, NY 10035 **The C-fragment of beta-lipotropin: an endogenous neuroleptic or antipsychotogen?** Science. 194(4265):632-635, 1976.

The C-fragment of beta-lipotropin, also called beta-endorphin, was microinjected into the periaqueductal gray of male albino rats weighing 250 to 350gm. Other rats were given methionine/enkephalin, leucine/enkephalin, or alpha-endorphin. Rats were then tested for analgesia (pinch, pinprick, hotplate, and ice water), reflex action, sedation, immobility, and catalepsy. Two days later, animals were given microinjections of morphine to establish that the injection site was indeed a morphine sensitive site. None of the peptides had analgesic activity except for the C-fragment. Each of the four peptides had moderate to profound effects on reflexes, sedation, immobility, and catelepsy, with the C-fragment being most active. Naloxone reversed all behavioral effects of the C-fragment. Thus, the C-fragment offers the best fit for the receptor which mediates these physiological functions. The similarity of this behavior to that seen after systematic administration to experimental animals of exogenous neuroleptics suggests that a disturbance in the bioavailability of this neuropeptide to receptor sites in the brain (perhaps because of lack of enzymatic cleavage from the circulating parent hormone, beta-lipotropin) may be an etiological factor in those psychopathological states for which the exogenous neuroleptics exert an ameliorative influence. 21 references.

002268 Jakoubek, B.; Pavlik, A.; Kraus, M.; Rehulka, J. Institute of Physiology, Czechoslovak Academy of Sciences, 142 20 Praha 4, Czechoslovakia **Uptake of 3H-leucine into the brain and other organs during the conditioned reaction to painful stimulation; effect of diazepam.** Activitas Nervosa Superior (Praha). 18(1-2):139-141, 1976.

In a paper presented at the Fifth Symposium on Brain and Behavior Organized in Cooperation with Intermozg, held in Liblice, Czechoslovakia in June 1975, an investigation is reported on whether stress induced changes in macromolecular metabolism are specific for brain tissue, or unspecific in nature; uptake studies were also performed on other organs of the body. Male rats, 16 days old, were used, and the conditioned reaction to painful stimulation was elaborated in 16 animals. After six conditionings, eight rats with an elaborated conditioned reaction to painful stimulation were injected with 4,5-3H-L-leucine, and killed within forty five minutes. Results in changes of the radioactivity of the precursor pool, changes in the precursor product relation, and in the synthesis of proteins are discussed. 8 references.

002269 Jaques, R. Research Department, Pharmaceuticals Division, Ciba-Geigy Ltd., CH-4002 Basel, Switzerland **Beta-adrenergic blocking agents as potent antagonists of mescaline-induced contractions in the rat uterus.** Experientia (Basel). 32(8):1038-1039, 1976.

The inhibitory effect of beta-adrenergic stimulants and blockers on mescaline induced contractions in the rat uterus was studied. Uterine horns from virgin rats were placed in de Jalon's solution. The drug to be tested for antagonistic activity was added to the bath fluid 2 min before 10mcg/ml mescaline sulfate. The following drugs counteracted the contractions induced by mescaline: epinephrine and norepinephrine, beta-adrenergic stimulants (isoproterenol, terbutaline); beta-adrenergic blocking agents (D-oxprenolol, pronethalol); some pspychotropic drugs (chlorpromazine, amitriptyline, benzoctamine); and a serotonin antagonist (methysergide). Drugs inactive at moderate doses included anticholinergic drugs (atropine, scopolamine, oxyphenonium); antispasmodic drugs (papaverine, adipheinine); anti-adrenergic drugs (phentolamine, hydergine, dibenamine); antidepressants (imipramine, desipramine, maprotiline); an antihistaine (tripelennamine); and a local anesthetic (dibucaine). Antagonism of mescaline induced contractions does not parallel antagonism of serotonin induced contractions. 5 references.

002270 Kaariainen, Ilpo. Department of Pharmacology, University of Helsinki, Siltavuorenpenger 10, SF-00170 Helsinki 17, Finland **Effects of aminooxyacetic acid and baclofen on the catalepsy and on the increase of mesolimbic and striatal dopamine turnover induced by haloperidol in rats.** Acta Pharmacologica et Toxicologica (Kobenhavn). 39(3):393-400, 1976.

Effects of aminooxyacetic acid (AOAA) and baclofen on the catalepsy and on the increase of mesolimbic and striatal dopamine turnover induced by haloperidol were studied in rats. AOAA which increases the cerebral concentration of gamma-aminobutyric acid (GABA) and baclofen, a structural analogue of GABA, did not induce catalepsy by themselves but potentiated the catalepsy caused by haloperidol. AOAA and baclofen decelerated the dopamine disappearance caused by alpha-methyl-p-tyrosine (alpha MT) both in mesolimbic nuclei and striatum. The results support the earlier suggestions that GABAergic pathways have an inhibitory effect on the mesolimbic and striatal dopaminergic pathways. 19 references. (Author abstract modified)

002271 Kafoe, W. F.; De Ridder, J. J.; Leonard, B. E. Pharmacology Department, Organon International B.V., Oss, The Netherlands **The effect of a tetracyclic antidepressant compound, Org GB94, on the turnover of biogenic amines in rat brain.** Biochemical pharmacology (Oxford). 25(22):2455-2460, 1976.

The effect of a tetracyclic antidepressant compound, Org GB94, on the turnover of biogenic amines in rat brain was stu-

died. There does not appear to be a correlation between the increase in brain noradrenaline turnover and the concentration of the drug in the brain. The data demonstrate that a large biological variation occurs in the concentration of Org GB94 in plasma and brain 2 and 24 hr after the last chronic dose. Previous findings that Org GB94 increases the rate of depletion of noradrenaline, and to a lesser extent of dopamine, which occurs following the administration of the tyrosine hydroxylase inhibitor alpha-methyl-p-tyrosine are confirmed. Results also suggest that Org GB94 has an action on brain amine metabolism which appreciably differs from that of the tricyclic antidepressants of the imipramine type. 29 references.

002272 Kallman, Mary Jeanne Davis. University of Georgia, Athens, GA 30602 **Superior colliculus lesions and the subsequent effect on amphetamine and methylphenidate induced hyperactivity. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-29534 HC$15.00 MF$8.50 89 p.

Locomotor activity changes resulting from the effects of continuous ambient noise, two pharmacological stimulants (d-amphetamine sulfate and methylphenidate hydrochloride) and partial superior colliculus destruction were investigated in albino rats 24 days following surgery. Depth perception following the lesions was also examined. Administration of the stimulants and continuous ambient noise increased activity levels. Partial destruction of the superior colliculus obliterated the arousing effect of ambient noise, implicating superior colliculus involvement in arousal changes due to ambient noise. Lesioning of the superior colliculus potentiated the stimulant action of d-amphetamine but did not potentiate the effect of methylphenidate injection. Although the two stimulants may produce similar behavioral effects, these findings suggest different sites of action within the CNS. Visual cliff performance was impaired by superior colliculus damage, and the observed deficits were unrelated to activity changes characteristic of superior colliculus lesioned rats. (Journal abstract modified)

002273 Karasawa, Tadahiko; Furukawa, Kiyoshi; Yamamoto, Ikuko; Yoshida, Kouichi; Shimizu, Masanao. Research Laboratories, Dainippon Pharmaceutical Co. Suita, Osaka 564, Japan **Effects of theophylline on central monoamine neurons.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):101P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March 1976, a study of the effects of theophylline (T) on brain monoamine neurons in Wistar rats was reported. Intraperitoneal injection of T produced dose dependent increases in the brain levels of 3-methoxy-4-hydroxyphenylethylene glycol sulfate (MOPEG) and 5-hydroxyindoleacetic acid (5-HIAA) but the level of homovanillic acid was only slightly affected. Norepinephrine (NE), serotonin (5-HT) and dopamine (DA) concentrations were not modified by the same doses of T. The exponential disappearance of endogenous brain MOPEG or 5-HIAA with time after pargyline was not affected by prior administration of T, suggesting that the observed increase of both acid metabolites following T was not due to the inhibition of the acid transport system in the brain. T enhanced the increase in brain normetanephrine level which was induced by pargyline or by a combination of pargyline and imipramine without an appreciable change in 3-methyoxytyramine level. The results imply that T and probably other methylxanthines may cause a release of NE and 5-HT in the brain. In rats with unilateral lesions of the nigrostriatal DA pathway induced by 6-hydroxydopamine, T caused a rotational behavior towards the intact side. The rotation was strongly inhibited by the alpha-adrenoceptor blocking agent phenoxybenzamine, which was only weakly effective in inhibiting the rotation induced by L-DOPA or methamphetamine. (Author abstract modified)

002274 Karbowski, Michael James. Virginia Commonwealth University/Medical College of Virginia, Richmond, VA **A new micro-method for determining the effects of drugs on the turnover rate of acetylcholine. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-23717 HC$15.00 MF$8.50 137 p.

To investigate how centrally acting drugs may alter the function of cholinergic neurons in the different brain areas, an improved acetylcholine (ACh) turnover technique was developed and tested. It involves injection of a tracer dose of 3H-choline (Ch) and calculating the accumulation of newly synthesized ACh after various pulse times. The technique is basically similar to those being used to estimate the turnover rate of catecholamines and serotonin. The assay relies on observing that tetraphenylboron in heptanone is exquisitely sensitive in extracting microquantities of ACh and Ch from brain tissue. The procedure was used to separate and extract brain ACh and Ch from the radiolabeled Ch metabolite, phosphorylcholine (CP). Ch was then separated from ACh by converting Ch to CP using choline kinase prior to another tetraphenylboron extraction. It was then possible to determine the effect of delta9-tetrahydrocannabinol on the turnover rate of ACh. Results suggested that the technique may be useful in determining the effects of drugs on central cholinergic neurons and that it is an improvement over existing methods in that it is less expensive and more efficient in handling a large number of samples. (Journal abstract modified)

002275 Katagiri, Mizuho. Department of Psychiatry, Juntendo University School of Medicine, Tokyo, Japan **Ultrastructural changes of the rat cerebellum due to pentetrazol and phenobarbital administration -- in special references to the changes of synaptic vesicles associated with convulsive seizures.** Psychiatria et Neurologia Japonica (Tokyo). 78(9):611-628, 1976.

To clarify the mechanism of occurrence and suppression of convulsive seizures, an electron microscopic study of changes in the rat cerebellum due to pentetrazol and phenobarbital administration was carried out. Slight changes in the nuclei and microorganelles of the cerebellar nerve cells were observed during seizures. The cerebeller nerve cells with phenobarbital administration showed slight mitochondrial degeneration. During convulsive seizures, synaptic vesicles in the molecular layer of the cerebellum were gathered adjacent to the presynaptic membrane, decreased in number in the synaptic boutons, and the presynaptic area tended to show low electron density. There were no remarkable changes in the neuroglia, blood vessels, and cerebellar glomerulus in either the pentetrazol or phenobarbital group. It was concluded that the changes noted in the number of the synaptic vesicles were more important than the degeneration of other neuronal elements in the cerebellum from the viewpoint of mechanism of occurrence and suppression of convulsive seizures. 58 references. (Author abstract modified)

002276 Katz, Richard J. Mental Health Research Institute, University of Michigan, Ann Arbor, MI 48109 **Effects of the cholinomimetic drug arecoline upon aggression: intra-vs. interspecific allocation of attack.** Aggressive Behavior. 2(3):205-212, 1976.

Systemic injections of cholinomimetic drugs have been reported to induce both rage and predatory attack in several spe-

cies. In order to assess the relative contribution of each of these two behavioral patterns in the control of cholinergically induced attack, a group of adult female cats was chemically stimulated with atropine and arecoline in the simultaneous presence of both a prey object and a conspecific attack object. In this choice situation stimulated cats initially tended to engage in rage attack. When a second group of subjects was tested in a successive choice situation a significantly greater number of attacks occurred against conspecifics. The results suggest that cholinergic stimulation initially induces affective attack, with somewhat less frequent incidents of predation. 19 references. (Journal abstract)

002277 Kawamura, Kohji; Kobayashi, Masafumi; Sato, Mikio. Department of Pharmacology, Nihon University School of Dentistry, Tokyo 101, Japan **Aggressive behavior, brain noradrenaline content and tyramine uptake of isolated mice -- effects of chronic administration of L-DOPA and safrazine.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):106P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March 1976, a study of the effects of chronic administration of L-DOPA and safrazine (a monoamine oxidase inhibitor, MAOI) on aggressive behavior, brain noradrenaline (NA) content and tyramine uptake in isolated mice was reported. Aggressiveness of isolated mice treated with L-DOPA plus MAOI was considerably higher at first enhancement but lower at second enhancement than that of isolated saline controls. Tyramine uptake in aggressive mice, particularly those given L-DOPA plus MAOI, was lower than the uptake levels determined in nonaggressive or aggregated mice. In comparison with aggregated mice, NA levels in mice maintained in isolation for 1 week were higher but the turnover was lower. NA turnover decreased in mice treated with L-DOPA plus MAOI as compared to NA turnover in saline treated controls. (Author abstract modified)

002278 Kellar, Kenneth J.; Elliott, Glen R.; Holman, R. Bruce; Vernikos-Danellis, Joan; Barchas, Jack D. Department of Pharmacology, Georgetown University School of Medicine and Dentistry, Washington, DC 20007 **Tryptoline inhibition of serotonin uptake in rat forebrain homogenates.** Journal of Pharmacology and Experimental Therapeutics. 198(3):619-625, 1976.

The effects of six tryptolines (tetrahydro-beta-carbolines) on 5-hydroxyryptamine (5-HT) uptake into rat forebrain homogenates were investigated. All six compounds were competitive inhibitors of 5-HT uptake. The most potent inhibitor was 5-hydroxytryptoline. Both 5-hydroxytryptoline and 5-hydroxymethtryptoline were relatively selective against 5-HT uptake being 20 times less potent against norepinephrine uptake and 40 times less potent against dopamine uptake. Because tryptolines may be formed as a result of alcohol consumption, it is suggested that the possibility that such compounds mediate some of the effects of alcohol on serotonergic pathways should be examined. 22 references. (Author abstract modified)

002279 Keller, William J.; Ferguson, Gary G. Department of Pharmacy, College of Pharmacy, University of Illinois Medical Center, Chicago, IL 60612 **Selectivity of 4-methoxyphenethylamine derivatives as inhibitors of monoamine oxidase.** Journal of Pharmaceutical Sciences. 65(10):1539-1543, 1976.

The inhibiting actions of various 4-methoxyphenethylamine derivatives on rat brain monoamine oxidase were studied in vitro. It was found that the oxidative deamination of tyramine by monoamine oxidase is inhibited by racemic 4-methoxy-beta-hydroxyphenethylamine and its N-methylated derivatives and that this series of compounds does not inhibit the action of monoamine oxidase when tryptamine is used as the substrate. In contrast, 4-methoxyphenethylamine and its N-methylated homologs inhibit the monoamine oxidase catalyzed deamination of both tyramine and tryptamine. 11 references. (Author abstract modified)

002280 Kempf, E.; Gill, M.; Mack, G.; Mandel, P. Centre de Neurochimie du CNRS, F-67085 Strasbourg Cedex, France **Effects of acute morphine administration on the catecholamine metabolism of three strains of mice.** Psychopharmacology Communications. 2(3):241-250, 1976.

The effects of acute morphine administration on the catecholamine metabolism of three strains of mice was investigated. Inbred mouse strains exhibited differences in motor activity and brain catecholamine metabolism after acute morphine injections. The two strains which increased motor activity after morphine also presented an increased noradrenaline turnover in the pons medulla, whereas no differences were found in the strain whose motor activity was unchanged. A correlation seems to exist between motor activity and the noradrenaline metabolism in the brainstem. 22 references. (Author abstract)

002281 Kisara, Kensuke; Shima, Keisetsu; Sakurada, Shinobu; Anezaki, Ken; Nakahama, Hiroshi. Department of Chemical Pharmacology, Tohoku College of Pharmacy, Sendai 983, Japan **The effect of morphine on single unit activity of midbrain dorsal raphe in cats.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):119P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March 1976, a study of the effect of morphine on single unit activity of midbrain dorsal raphe nucleus neurons of the cat was reported. Dorsal raphe neurons were divided into two types; one was a clock like neuron (CLN), and the other was nonclock like neuron (NCLN). The discharges of CLN were typically slow in rate, rhythmic, and stable across time, while those of NCLN were relatively irregular in pattern as compared with CLN. All 11 CLN were not reponsive to noxious (pinch and/or bradykinin) or nonnoxious (tap, hair, puff, light and/or sound) stimuli. Seven of ten NCLN were responsive to both noxious and nonnoxious stimuli, and three were not responsive to these stimuli. After morphine administration, all NCLN activated by noxious and innoxious stimuli became unresponsive to noxious stimuli but responsded to innoxious stimuli. Although firing frequency and pattern of CLN were unaffected, the firing frequency of NCLN was decreased after morphine administration. These results do not support the hypothesis that morphine enhances the activity of the raphe/spinal descending inhibitory system, the terminal of which inhibits pain transmission in the spinal cord. (Author abstract modified)

002282 Klygul', T. A. Institut farmakologiya AMN SSSR, Moscow, USSR **/Traits of the development of a tolerance for nitrazepam and phenobarbital under experimental conditions./** Osobennosti razvitiya tolerantnosti k nitrazepamu i fenobarbitalu v eksperimente. Farmakologiya i Toksikologiya (Moskva). 39(5):532-537, 1976.

A study was done of tolerance toward nitrazepam (neozepam), in its extended use, on different phenomena of activity in combination with tranquilizers of the benzdiazepine type and phenobarbital in experiments with rats and mice in conflict situations, with corazol induced convulsions, or with

induced lack of motor coordination. Extended injection of nitrazepam in mice and rats in constant and increasing doses resulted in development of tolerance relative to muscle relaxing and anticonvulsive effects, and development of lethality with no weakening in tranquilizer effect. Long-term treatment with phenobarbital lessened tranquilizing effect and reduced muscle relaxing effect. 16 references.

002283 Kocherga, V. Y. Institut biokhimii im. A. V. Palladina AN USSR, Kiev, USSR /**Neurochemical mechanisms of tricyclic antidepressants of the imipramine group.**/ Neyrokhimicheskie mekhanizmy deystviya tritsiklicheskikh antidepressantov gruppy imipramina. Ukrains'kiy Biokhimichniy Zhurnal (Kiev). 48(4):656-667, 1976.

Neurochemical mechanisms of tricyclic antidepressants of the imipramine group are discussed. These antidepressants mainly influence the neurotransmitter metabolism in the synapses, the activity of enzymatic systems regulating the transport of ions and the system of cyclic AMP metabolism. The interaction of tricyclic antidepressants with the membrane, and the resulting disturbance in reuptake of the transmitters epinephrine and 5-hydroxytryptamine in the neurons, is assumed to be one of the mechanisms of synaptic transmission regulation. The role of the antidepressant effect of tricyclic antidepressants in the inhibition of biological amine deamination, particularly phenylethylamine, is discussed. It is suggested that the thymoanaleptic effects of these antidepressants are due to activation of central serotoninergic processes, and their psychoanaleptic effect due to activation of the adrenergic system. Inhibition of Na-KATPase activity of the neural membranes may be one of the biochemical mechanisms regulating the tranquilizing effects of the tricyclic antidepressants. 135 references. (Journal abstract modified)

002284 Kohno, Yasuko; Nishikawa, Tadashi; Sano, Takayasu; Nagasaki, Nobuyuki; Furukawa, Tatsuo. Department of Pharmacology, Kurume University School of Medicine, Kurume 830, Japan **Effect of L-dopa on serotonin metabolism in rat brain: precursor tryptophan levels in various tissues.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):53P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study of the effect of L-dopa on serotonin (5-hydroxytryptamine, 5-HT) metabolism in rat brain was reported. Tryptophan (trp) concentrations in peripheral and brain tissues at various times after L-dopa administration to Wistar male rats were examined. L-dopa elicited a marked reduction of trp in the plasma and the kidney, an increase in trp liver, and a slight increase in brain trp. The same treatment produced a significant decrease in the brain content of 5-HT and an increase of 5-hydroxyindoleacetic acid (5-HIAA) content. Brain dopamine (DA) level was elevated but norepinephrine concentration was not notably affected. DA did not modify brain trp, 5-HT or 5-HIAA levels, but exhibited peripheral effects similar to those seen with L-dopa. After administration of L-dopa to newborn rats, the changes of brain 5-HT and 5-HIAA levels were similar to those in adult rats but the levels of trp in liver and kidney did not change. With a concomitant application of L-dopa and Ro4-4602, the reduction of cerebral 5-HT content was potentiated while changes of peripheral trp were reduced. It is suggested that the decreasing effect of L-dopa on plasma free trp has no obvious relationship to brain trp levels and that L-dopa reduces brain 5-HT level indirectly via the level of tryptophan. (Author abstract modified)

002285 Koldayev, V. M. Vladivostokskiy meditsinskiy institut, Vladivostok, USSR /**Effect of some analeptics on the outcome of acute microwave lesions in mice.**/ Vliyaniye nekotorykh analeptikov na iskhod ostrogo mikrovolnovogo porazheniya myshey. Farmakologiya i Toksikologiya (Moskva). 39(5):543-544, 1976.

The effect of different analeptics on the outcome of microwave shock to terminal state was studied in experiments on 623 mice. Controls were given medicinal substances. The animals were given single injections of analeptics immediately after the shock and calculations of effectiveness were based on the number of animals surviving over a period of 3 weeks in relation to number of mice in each group. Strychnine and nicotinic diethylamide were found to be effective, while cytisine, camphor, caffeine, corasol, and lobeline were ineffective. 4 references.

002286 Komendantova, M. V.; Pashuk, L. K. Moskovskiy meditsinskiy stomatologicheskiy institut im. N. A. Semashko, Moscow, USSR /**Effect of aminazine and promedol on delayed hypersensitivity and pharmacodynamic changes in these substances in the given pathology.**/ Deystviye aminazina i promedola na giperchuvstvitel'nost' zamedlennogo tipa i izmeneniye farmakodinamiki etikh veshchestv pri dannoy patologii. Farmakologiya i Toksikologiya (Moskva). 39(2):137-141, 1976.

A study was made to determine the effect of neurotropic substances, aminazine (chlorpromazine) and promedol (trimeperidin), on the formation of lymphoblasts, and pharmacodynamic changes of these substances in a delayed allergy. Rabbits were injected with egg albumin to produce a slow allergic reaction. A lymphocyte culture was prepared with blood from the experimental group and a control group of intact rabbits, and the percentage of lymphoblasts in both samples was established. After addition of aminazine and promedol, lymphoblast formation was intensified with phytohemaglutinin. Indices of delayed allergy dropped with aminazine, but increased with promedol. The different effects of these substances occurred both when they were added to the culture of lymphoid cells and when they were injected into animals with delayed hypersensitivity. Pharmacological changes occurred in both aminazine and promedol, the analgesic effect was lowered in allergy of the delayed type. 20 references.

002287 Korolenko, T. A.; Tsilli, E. I.; Rusova, T. V. Novosibirskiy meditsinskiy institut, Novosibirsk, USSR /**Effect of mellaril on liver lysosomes in rats with acute toxic hepatitis.**/ Vliyaniye mellerila na lizosomy pecheni krys s ostrym toksicheskim gepatitom. Farmakologiya i Toksikologiya (Moskva). 39(4):467-470, 1976.

Because liver damage due to phenothiazines is a limiting factor in their use, a study was made of the pharmacological heterogeneity of liver lysosomes through comparative investigation of heavy and light lysosomes following administration of the relatively nontoxic phenothiazine mellaril to intact rats and rats with acute toxic hepatitis induced by carbon tetrachloride. Results showed: 24 hours after mellaril injection of intact rats there was an increase in vulnerability to damage due to both types of lysosomes, and in rats with toxic hepatitis mellaril treatment depressed free activity of acid phosphatase in both types of lysosomes, and the light lysosomes showed less sensitivity to the effect of the hypotonic agent. 11 references.

002288 Kuriyama, Kinya; Yoneda, Yukio. Department of Pharmacology, Kyoto Prefectural University of Medicine, Kyoto 602, Japan **Alterations in distribution and metabolism of gamma-aminobutyric acid (GABA) in the central nervous system following morphine administration.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):18P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study of the alterations in distribution and metabolism of gamma-aminobutyric acid (GABA) in the central nervous system following morphine administration was reported. Morphine increased the GABA content in the dorsal horn and surrounding areas of the central canal of the rat spinal cord. This effect was antagonized by levallorphan. Similarly morphine increased the GABA content of thalamic nuclei. Sodium salicylate and pentazocine increased GABA only in the nucleus reuniens thalami. Aminooxyacetic acid (AOAA) potentiated morphine analgesia while semicarbazide and bicucullini inhibited the analgesic response. The results suggest that the functional alterations of GABA containing neurons involved in pain perception may play a role in the induction of morphine analgesia by increasing inhibitory input at the spinal cord and thalamus. (Author abstract modified)

002289 Kurochkin, I. G.; Tsikalova, T. S. Laboratoriya farmakoterapii ekstremal'nykh sostoyaniy, otdela farmakologii Instituta farmakologii AMN SSSR, Moscow, USSR **/Peculiarities of the action of sodium oxybutyrate, amphetamine, transamine and l-dopa on physical performance capacity of animals under multiple load conditions./** Osobennosti vliyaniya oksibutirata natriya, fenamina, transamina, l-dofa na fizicheskuyu rabotosposobnost' zhivotnykh v usloviyakh mnogokratnykh nagruzok. Farmakologiya i Toksikologiya (Moskva). 39(6):656-658, 1976.

In an extension of earlier research in which it was found that sodium oxybutyrate, amphetamine or l-dopa restored physical performance capacity of rats after a single exhaustive exertion, a study was made of the specific action of these compounds, plus transamine, on the dynamics of restoration of physical capacity after multiple loads. Results showed that transamine alone or in combination with sodium oxybutyrate accelerated complete restoration of physical capacity after a single test of exertion. Transamine in combination with amphetamine increased performance capacity, but this was followed by marked depletion of the recovery process under subsequent loads. Sodium oxybutyrate in combination with l-dopa produced a prolonged increase in performance capacity under multiple loading. 5 references. (Journal abstract modified)

002290 Kurtsin, I. T.; Kuznetsova, E. K. Laboratorii kortikovistseral'noy fiziologii i patologii, Instituta Fiziologii im. I. P. Pavlova AN SSSR, Leningrad, USSR **/Effects of neurotropic substances on secretion and blood supply of the pancreas./** Vliyaniye neyrotropnykh sredstv na sekretsiyu i krovosnabzheniye podzheludochnoy zhelezy. Farmakologiya i Toksikologiya (Moskva). 39(6):665-667, 1976.

Chronic experiments with dogs demonstrated that chlorpromazine and caffeine inhibit pancreatic activity, while amphetamine stimulates pancreatic activity. Fourfold higher doses of amphetamine did not significantly change pancreatic function, while a twentyfold higher dose of amphetamine produced a biphasic effect, with secretatory excitation being followed by inhibition. 7 references. (Journal abstract modified)

002291 Kuschinsky, K.; Noring, R.; Ulmar, G. Department of Biochemical Pharmacology, Max-Planck-Institute for Experimental Medicine, Hermann-Rein-Str. 3, D-34 Gottingen, Germany **Effects of opiates on GABA and dopamine metabolism in the nigro-striatal pathways of rats.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 294(Supplement):R14, 1976.

In a paper presented at a pharmacology meeting in Hannover, Germany, September 14-17, 1976, the effects of opiates on gamma-aminobutyric acid (GABA) and dopamine metabolism in the nigrostriatal pathways of rats were reported. In rats, narcotic analgesics decrease dopaminergic neurotransmission, resulting in catalepsy and muscular rigidity, and increase the dopamine turnover in the corpus striatum. In morphine withdrawal, when alterations of the dopamine metabolism were evident, no changes in GABA concentration or glutamate decarboxylase activity could be detected, neither in the corpus striatum nor in the substantia nigra, compared with control animals. (Author abstract modified)

002292 Lal, Harbans; Miksic, Stephen; Drawbaugh, Richard; Numan, Robert; Smith, Nelson. Dept. of Pharmacology and Toxicology, College of Pharmacy, University of Rhode Island, Kingston, RI 02881 **Alleviation of narcotic withdrawal by conditional stimuli.** Pavlovian Journal of Biological Science. 11(4):251-262, 1976.

Alleviation of narcotic withdrawal syndrome by conditional stimuli was studied in rats to ascertain that if a morphine like pharmacological action can be produced by conditional stimuli (CS), then these CS may mimic the action of narcotic drugs in blocking narcotic withdrawal. Auditory, olfactory, and social stimuli were systematically paired with each injection of morphine in the rats. It was found that, when morphine was kept constant at a low dose, the external stimuli acquired the property of a CS to cause hypothermia which was antagonized by naloxone. In rats in which morphine doses were regularly increased to cause morphine dependence, with the CS presented during withdrawal, caused reduction in withdrawal signs (wet shakes, hypothermia, aggression) and produced hyperglycemia as well as elevation of striatal homovanillic acid. CS induced alleviation of withdrawal hypothermia was blocked by mecamylamine, phenoxybenzamine, heloperidol, benzatropine or naloxone but not by cyproheptadine or propranolol. It was concluded that any effective therapeutic program for the treatment of narcotic abuse should thoroughly extinguish the conditioned effects of environmental stimuli associated with both drug administration and abstinence syndrome. 23 references. (Author abstract modified)

002293 Lapin, I. P. Laboratory of Psychopharmacology, Bekhterev Psychoneurological Research Institute, Leningrad 193019, USSR **Depressor effect of kynurenine and its metabolites in rats.** Life Sciences (Oxford). 19(10):1479-1484, 1976.

To elucidate the depressor effects of kynurenine and its metabolites, rats were injected with 3-hydroxykynurenine, 3-hydroxyanthranilic acid, anthranilic acid, nicotinic acid, quinolinic acid, or picolinic acid; and physiological responses were monitored. Kynurenine in doses of 0.2ng to rats weighing 160 to 240g elicited a measurable decline in blood pressure. The depressor effect increased with dosage and reached a maximum of about 30 mm Hg at a dose of approximately 100 micrograms. At higher doses (400 to 2000) micrograms kynurenine elicited a pressor response of about 15 mm Hg. Other kynurenines tested also lowered blood pressure. It is possible that the increased formation of kynurenine and its metabolites

is involved in disturbances of circulation under stress, when the formation of these compounds is increased by activation of liver tryptophan pyrrolase. 4 references. (Author abstract)

002294 Laudenslager, M. L. Scripps Institution of Oceanography, Physiological Research Lab, A-004, La Jolla, CA 92093 **The influence of hypothalamic temperature on some thermoregulatory effects of hypothalamic injections of norepinephrine.** Pharmacology Biochemistry and Behavior. 5(6):713-716, 1976.

To investigate the influence of hypothalamic temperature on the behavioral thermoregulatory effects on preoptic anterior hypothalamus injections of norepinephrine in the squirrel monkey, reactions to variations of ambient temperature and hypothalamic temperatures were observed. Bilateral injections of norepinephrine bitartrate into the preoptic region and anterior hypothalamus were always followed by a reduction in core temperature and rate of behaviorally obtaining radiant heat in cold exposed (5 degree C) squirrel monkeys regardless of whether the temperature of this region was experimentally raised (40 to 42 degree C) or lowered (32 to 34 degree C). Decreases in tail temperature following injections of norepinephrine indicated that vasoconstriction was also associated with the reduction in body temperature and behavioral responses. Since conflicting behavioral and autonomic responses are observed following injections of norepinephrine. It is suggested that norepinephrine may be affecting thermoregulatory effector pathways nonspecifically rather than altering the set point about which body temperature is regulated. 10 references. (Author abstract modified)

002295 Lavretskaya, E. F.; Libinzon, R. Ye.; Mal'dov, D. G.; Ratnikova, L. A.; Chistyakov, V. V.; Chugunov, V. V. Nauchno-issledovatel'skiy institut po biologicheskim ispytaniyam khimicheskikh soyedineniy, noc. Staraya Kupavna, Moskovskoy oblasti, USSR /**Some effects of interaction of psychotropic and anticonvulsant agents.**/ Nekotorye effekty vzaimodeystviya psikhotropnykh i protivosudorozhnykh sredstv. Zhurnal Nevropatologii i Psikhiatrii Imeni S. S. Korsakova (Moskva). 76(8):1228-1231, 1976.

The interaction of phenobarbital with chlorpromazine, melipramine, and chlordiazepoxide was studied in Wistar rats weighing 150 to 200g. Phenobarbital in a dose of 80mg/kg increased the RNA and protein content of liver, as did 50mg/kg chlordiazepoxide. Both phenobarbital and chlordiazepoxide increased hepatic oxidation of amidopyrine and hexobarbital and increased the liver content of cytochrome P-450. Chlorpromazine and melipramine did not affect any of these measurements but did alter the affinity of P-450 cytochrome to amidopyrine and hexobarbital and the speed of oxidation of these substrates. Repeated use of phenobarbital and chlordiazepoxide weakens the pharmacological effect of many medications. 16 references.

002296 Lehne, Richard Albert. George Washington University, Washington, DC **A study of the effect of benzodiazepines on cyclic nucleotide metabolism as related to neuronal activity in the bullfrog sympathetic ganglion. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-22981 HC$15.00 MF$8.50 223 p.

To study the effect of benzodiazepines on cyclic nucleotide metabolism as related to neuronal activity in the bullfrog (Rana catesbiana) sympathetic ganglion, the effects of one form of this antidepressant (diazepam) were measured in the isolated, stimulated, paravertebral sympathetic chain. The combination of diazepam plus stimulation was greater than additive on ganglionic cyclic adenosine 3',5'-monophosphate (cAMP), indicating potentiative synergism between diazepam and preganglionic stimulation. Diazepam mediated by postetanic potentiation inhibition and the cAMP elevation were correlated. Measurement of diazepam effects on the enzymes regulating cAMP metabolism revealed that the drug inhibited cyclic nucleotide phosphodiesterase (PDE) in homogenates of ganglion but did not stimulate adenylate cyclase activity. Detailed study of benzodiazepine mediated PDE inhibition indicated that the drugs were potent PDE II inhibitors whose Ki's varied markedly with subtle changes in drug structure. The Ki data suggested that benzodiazepines may have a greater impact on the physiology of cAMP mediated processes by inhibiting activated PDE II than by inhibiting nonactivated enzyme. No correlation betwen benzodiazepine Ki values and their in vivo anticonvulsant or anxiolytic potencies occurred. (Journal abstract modified)

002297 Leterrier, Francois; Mendyk, Alain; Viret, Jacques. Centre de Recherches du Service de Sante des Armees, 1 bis rue du Lieutenant Raoul Batany, F-92140-Clamart, France **Interaction of chlorpromazine with biological membranes: a photochemical study using spin labels.** Biochemical Pharmacology (Oxford). 25(22):2469-2474, 1976.

Fatty acid spin labels have been included into erythrocyte ghosts and synaptic plasma membranes in order to study the interaction of phenothiazine derivatives (particulary chlorpromazine) with these membranes. Results indicate: 1) weak modifications of the spin label spectroscopic response are observed only on the label of the polar part of the membrane and with chlorpromazine concentrations higher than 5 x 10-4 M; and 2) under ultraviolet irradiation (lamboda=310nm) phenothiazine derivatives reduce fatty acids spin labels. The photochemical interaction is influenced by the membrane proteins. Results suggest that, in the pharmacologically active concentration range, chlorpromzaine seems to localize at the interface between the phospholipids and the proteins of the membranes. 31 references. (Author abstract modified)

002298 Loh, Horace H.; Brase, David A.; Sampath-Khanna, Sumathy; Mar, Jeffrey B.; Way, E. Leong; Li, Choh Hao. Department of Pharmacology, University of California, San Francisco, CA 94143 **Beta-endorphin in vitro inhibition of striatal dopamine release.** Nature (London). 264(5586):567-568, 1976.

The inhibitory effect of beta-endorphin on striatal dopamine release from the central nervous system in vitro was studied. The abilities of morphine, betaendorphin and Metenkephalin to rat brain striatal slices preloaded with 3H-dopamine showed that beta-endorphin was twice as pot-ent as morphine. Met-enkephalin, however, did not produce a significant blockade of the inhibition by morphine and beta-endorphin, the blockage being more complete with morphine than for beta-endorphin. The results indicate an initial demonstration of the inhibition of dopamine release from central nervous system tissue by an endogenous opiate like peptide and suggest that the actions of beta-endorphin in the CNS are probably not limited to the inhibition of dopamine release alone. 19 references.

002299 Losev, N. A.; Myasnikova, Ye. M. Otdel farmakologii, Laboratoriya eksperimentalnoy farmakoterapii, Instituta eksperimental'noy meditsiny AMN SSSR, Leningrad, USSR /**Functional significance of the alpha and beta adrenoreceptors in the structures of the striopallidar system.**/ O funktsional'non znachenii alfa i beta adrenoretseptorov v strukturakh striopallidarnoy sistemy. Fiziologicheskiy Zhurnal SSSR (Leningrad). 62(4):510-515, 1976.

The functional significance of noradrenaline (N), isadrine (I), phentolamine, and propranol at dose level 0.1to 1.0mg in relation to the neuronal structures of the striatum was tested in 80 rabbits. It was found that N and I had inhibitive and stimulative effects. The experiments revealed antagonism between alpha and beta adrenomimetics. It is suggested that N compounds have a very important mediatory role in the adrenergic synapses of the stratium. The existence of alpha and beta adrenoreceptors in different parts of the brain is postulated. 33 references.

002300 Maj, J. Institute of Pharmacology, Polish Academy of Science, Krakow, Poland **Dopaminergic drug effects upon serotonin neurons.** In: Essman, W., Current developments in psychopharmacology. New York, Spectrum, 1976. 393 p. v. 3. (p. 55-83).

Studies in animals providing biochemical, histochemical, and electrophysiological evidence that various dopamine (DA) agonists exert an influence upon serotonin (5-HT) neurons are reviewed, with emphasis on the effects of apomorphine, L-DOPA, dimethylaminoadamantane, amphetamine, and piribedil. It has been found that DA agonists acting presynaptically or postsynaptically exert an effect on 5-HT neurons which is detectable by production of changes in the concentrations of 5-HT and/or 5-hydroxyindoleacetic acid in various brain regions and by their effects on pontogeniculo/occipital (PGO) activity evoked by Ro 4-1284 or by parachlorophenylalanine. Some of the agonists (L-DOPA and possibly amphetamine) appear to have a primary influence on 5-HT neurons, while others (apomorphine) produce secondary effects on 5-HT neurons resulting from the primary stimulation of DA receptors. The hypothesis that a dopaminergic/serotonergic interaction exists in the central nervous system, and some of the implications of this hypothesis for various pharmacological and behavioral effects produced by DA agonists, are briefly discussed. 194 references.

002301 Mao, C. C.; Marco, E.; Revuelta, A.; Costa, E. Laboratory of Preclinical Pharmacology, National Institute of Mental Health, Saint Elizabeths Hospital, Washington, DC 20032 **Antipsychotics and GABA turnover in mammalian brain nuclei. (Unpublished paper).** Rockville, MD, NIMH, 1976. 23 p.

The involvement of gamma-aminobutyric acid (GABA) neurons in the pharmacological actions of neuroleptic drugs was studied by measuring the turnover of GABA in the substantia nigra, globus pallidus, nucleus accumbens, and nucleus caudatus after injection of various antipsychotic drugs. Haloperidol, pimozide, thioridazine and clozapine increased the turnover of GABA in nucleus accumbens and globus pallidus. Thioridazine and clozapine failed to cause extrapydramidal side effects or tardive dyskinesia and increased GABA turnover in nucleus caudatus and substantia nigra. Pimozide and haloperidol produced extrapyramidal side effects and tardive dyskinesia and did not affect the turnover of GABA in substantia nigra. The turnover of GABA in nucleus caudatus was not affected by pimozide but was reduced by haloperidol. It is suggested that an increase in GABAergic function in nucleus accumbens and globus pallidus may be associated with antipsychotic activity and that those antipsychotics which increase GABA turnover in the striatonigral system may be devoid of extrapyramidal side effects and tardive dyskinesia. 35 references. (Author abstract modified)

002302 Maruyama, Shoji; Kawasaki, Tadashi. Dept. of Neurophysiology, Brain Research Inst., Niigata Univ., Niigata 951, Japan **Further electrophysiological evidence for the GABA-like effect of droperidol in the Purkinje cells of the cat cerebellum.** Japanese Journal of Pharmacology (Kyoto). 26(6):765-767, 1976.

The interaction between droperidol or chlorpromazine and imidazole acetic acid which is known to act on the same group of receptors as GABA (2-4) or glicine which is reported to depress the firing rate of Purkinje cells in the cat cerebellum was investigated. Experiments were carried out on 34 adult cats. The depressant effect of glycine was found to be enhanced in about half the number of Purkinje cells tested, and to be unaffected in the remaining by the concurrent release of droperidol; depression produced by glycine was not blocked by the concurrent release of bicuculline in all cells tested. The mechanism of the depressant action of glycine is apparently different from that of droperidol. It is concluded that chlorpromazine does not act on the GABA operated synapses and does not affect glycine sensitive neurons. 7 references.

002303 Maslinski, C.; Ciesielska, J.; Lebrecht, U.; Nowak, J. Z. Biogenic Amines Department, Polish Academy of Sciences, Narutowicza 60, 90-136 Lodz, Poland **The influence of H1 and H2 histamine receptor antagonists on histamine metabolism in rat brain.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 294(Supplement):R29, 1976.

In a paper presented at a pharmacology meeting in Hannover, Germany, on September 14-17, 1976, the influence of H1 and H2 histamine receptor antagonists on histamine metabolism in rat brain was described. Focus was on the action of metiamide, burimamide, mepyramine, and amodiaquine on histamine-methyltransferase in vitro and in vivo. The results indicate that each antihistamine drug was a selective antagonist of histamine metabolism both as to site of inhibition and dosage level at which inhibition was made manifest. (Author abstract modified)

002304 Mayevsky, A. Bar-Ilan University, Ramat Gan, Israel **Metabolic and electrical responses of the brain to complete ischemia in the awake and anesthetized rat.** Israel Journal of Medical Sciences (Jerusalem). 12(12):1525, 1976.

A summary of a paper delivered at the 36th meeting of the Israel Physiological and Pharmacological Society on metabolic and electrical responses of the brain to complete ischemia in the awake and anesthetized rat is presented. To evaluate changes in the metabolic state of the brain of the awake, and the anesthetized with pentrobarbital or with urethan rat, at the moment of and after decapitation, the time sharing fluorometer reflectometer which measures oxidation reduction state of NADH was used. After decapitation the NADH started to increase with 1 sec in the awake rat while in the anesthetized rat the increase was delayed by 1 to 2 sec. The electrocorticogram disappearance was significantly faster in the awake rat as was the rate of NADH increase. This methodology for studying brain ischemia is suggested for testing of anesthetics on brain metabolism.

002305 Maysov, N. I.; Tolmacheva, N. S.; Rayevskiy, K. S. Institut farmakologii AMN SSSR, Moscow, USSR **/Liberation of 3H-GABA from isolated nerve endings of the rat cortex under the effect of psychotropic agents./** Vysvobozhdeniye 3H-gamk iz izolirovannykh nervnykh okonchaniy kory mozga krys pri deystvii psikhotropnykh veschestv. Farmakologiya i Toksikologiya (Moskva). 39(5):517-520, 1976.

A study was made of the role of 3H-gammaaminobutyric acid (3H-GABA) as an inhibitory mechanism, and its liberation from presynaptic nerve endings in the rat cortex under the effect of psychotropic drugs. Work was done in vitro using a saccharose solution. The neuroleptics aminazine (chlorpromazine) and phthorphenazine intensified liberation of 3H-GABA from cortical synapses of the rat brain. The neuroleptic trifluperidol and the antidepressants imipramine and phthoracizine had similar but less marked effects. Azabuperon, carbidine, and diphenylhydantoin restricted liberation. Diazepam, gamma oxybutric acid, and carbamazepine had no effect. The effects of the psychotropic drugs are due to their direct influence on the synaptic membrane. 14 references. (Author abstract modified)

002306 Mayzelis, M. Ya. Moskovskiy institut psikhiatrii Ministerstva zdravookhraneniya RSFSR, Moscow, USSR **/Effect of repeated application of aminazine, majeptil, and trisedyl on protein synthesis in different structures of the rat brain./** Vliyaniye kursovogo primeneniya aminazina, mazheptila i trisedila na sintez belka v raznykh strukturakh mozga krys. Farmakologiya i Toksikologiya (Moskva). 39(4):411-413, 1976.

A study was made of absorption of tagged amino acids by protein in different sections of the brain in experimental animals following sequential injections of aminazine (chlorpromazine), majeptil, and trisedyl. Over a course of 20 days, 60 male rats were given doses of the drugs sufficient to produce a neuroleptic effect, and then were given a solution of radioactive methionine. Radioactivity was measured per gram of protein and gram of body weight. Aminazine, majeptil, and trisedyl lowered the level of methionine in protein in most sections of the brain. In the hemispheres, basal ganglia and cerebellum, synthesis of protein was somewhat facilitated, but the changes were statistically doubtful. Multiple injections of aminazine and trisedyl had less effect on protein synthesis than a single injection. 7 references.

002307 McCandless, David W.; Curley, Alison D.; Cassidy, Carol E. Department of Anatomy, University of Vermont, College of Medicine, Burlington, VT 05401 **Thiamin deficiency and the pentose phosphate cycle in rats: intracerebral mechanisms.** Journal of Nutrition. 106(8):1144-1151, 1976.

The effect of decreased transketolase levels on the activity of the pentose phosphate cycle in murine thiamin deficient cortex and brainstem was studied. Cortices and brainstems from thiamin deficient and control rats were analyzed for activity of the two regulatory enzymes of the pentose phosphate cycle, glucose-6-phosphate dehydrogenase and 6-phosphogluconate dehydrogenase. In both the brainstem and cortex of thiamin deficient rats, areas in which transketolase activity was decreased up to 65%, the activities of the two regulatory enzymes, were unaltered. Furthermore, flux through the pentose phosphate cycle was not decreased as compared to pair fed control rats. These data do not support the hypothesis that in thiamin deficient rats a decrease in cerebral transketolase activity leads to a diminished pentose phosphate cycle activity. 24 references. (Author abstract modified)

002308 Meier-Ruge, W.; Iwangoff, P. Basic Medical Research Department, Sandoz Ltd., CH-4002, Basle, Switzerland **Biochemical effects of ergot alkaloids with special reference to the brain.** Postgraduate Medical Journal (Oxford). 52(Supplement 1):47-54, 1976.

In a paper presented at a symposium on ergot compounds in London in May 1975, the biochemical effects of dihydrogenated ergot alkaloids on the central nervous system were reported. With the exception of dihydroergotoxine distribution studies, the biochemical investigations were performed in vitro on cat and beef brain. Dihydroergotoxine (Hydergine) effects on brain metabolism are suggested from distribution studies. Microhistoautoradiographically an accumulation of DH-ergotoxine in neuronal cells of the reticular formation and the hypothalamus was observed. Cell gradient centrifugation studies demonstrated a 60% DH-ergotoxine accumulation in the synaptic fraction, whereby influences on metabolic turnover and electrical transmission of the neuronal cell can be expected. DH-ergotamine, DH-ergotoxine and DH-ergonine especially are believed to: inhibit catecholamine reuptake, decrease catecholamine activation of sodium/potassium adenosinetriphophatose, inhibit catecholamine activated adenylcyclase to its initial level, and cause brain specific inhibition of cAMP-phosphodiesterase (low Km phosphodiesterase), which preserves the functionally important basal cAMP level in the neuronal cell. All these effects on enzymes influencing the balance between ATP splitting and ATP synthesis moderate the energy turnover and in this way the function of the brain. DH-ergotoxine inhibits the activity of the low Km phosphodiesterase, the enzyme which splits the cAMP regulating basal neuronal function. This suggests that DH-ergotoxine improves the homeostatic equilibrium of the neuronal cell. These biochemical findings may substantiate previous experimental studies with ischemic and hypovolemic brain lesions. 34 references. (Author abstract)

002309 Mellerup, Erling T.; Plenge, Per. Psychochemistry Institute, University of Copenhagen, Rigshospitalet, 9, DK-2100 Copenhagen, Denmark **Lithium effects on magnesium, calcium, and phosphate metabolism in rats.** International Pharmacopsychiatry (Basel). 11(3):190-195, 1976.

To determine the effects of lithium on magnesium, calcium, and phosphate metabolism in rats, 20 rats were treated with lithium chloride for 8 weeks, and then given radioactive calcium, magnesium, and phosphate on the last day of treatment. Electrolyte content and radioactivity were determined in serum, bone, muscle, liver, and brain. Lithium led to an increase of inorganic phosphate in muscle and a decrease in serum. Uptake of radioactive phosphate was increased in muscle and liver, but reduced in bone. The amount of magnesium in muscle and serum was increased in the lithium treated rats, while the uptake of radioactive magnesium into bone was decreased. Uptake of radioactive calcium into bone was reduced, and radioactive calcium in serum was increased after lithium. The possible relationship between the effects of lithium on carbohydrate, phosphate, calcium and magnesium metabolism in the rat and the relapse preventive effect of the drug in humans is briefly discussed. 20 references. (Author abstract modified)

002310 Meltzer, Herbert Y.; Fang, Victor S. Department of Psychiatry, University of Chicago, Pritzker School of Medicine, 950 E. 59th. St., Chicago, IL 60637 **Effect of apomorphine plus 5-hydroxytryptophan on plasma prolactin levels in male rats.** Psychopharmacology Communications. 2(3):189-198, 1976.

The relative potency of dopaminergic inhibition and serotonergic stimulation of prolactin secretion in male rats was compared. 5-Hydroxytryptophan (5-HTP), the precursor of serotonin, produced a 6 to 11 fold increase in plasma prolactin. Apomorphine, a dopamine agonist, had no significant effect on plasma prolactin. However, when apomorphine was given with or before 5-HTP, it nearly completely blocked the increase in

prolactin produced by 5-HTP. These results indicate that inhibition of prolactin produced secretion by dopaminergic stimulation can overcome the prolactin releasing effect of serotonin. The results are consistent with the hypothesis that prolactin secretion is ordinarily under a weak serotonergic stimulation and a profound dopaminergic inhibition. It is also possible that apomorphine affects plasma prolactin levels by increasing prolactin clearance. 25 references. (Author abstract)

002311 Meyer, D. R.; Sparber, S. B. Department of Pharmacology, University of Minnesota, Minneapolis, MN 55455 **A comparison of withdrawal in rats implanted with different types of morphine pellets.** Pharmacology Biochemistry and Behavior. 5(6):603-607, 1976.

To compare the variability of the duration and severity of physical drug dependence induced by 3 types of morphine (M) pellets varying in surface area and hardness, rats were subcutaneously implanted with one of the 3 types of pellets formulated according to the method of Gibson and Tingstad. Animals were maintained for 19 days after implanation and physical dependence was assessed every other day. Severity of naloxone induced withdrawal was quantified by the use of a composite symptom score and weight loss. Withdrawal severity was greatest following implantation of a pellet (Type C) of large surface area and low hardness rating, and least following implantation of a pellet (Type A) of small surface area and high hardness rating. Abstinence severity which resulted from implantation of a pellet (Type B) of moderate surface area and low hardness rating was intermediate. When 2 pellets were implanted the difference between Type C and B was amplified. It was concluded that formulation per se was not sufficient for specifying morphine pellet characteristics. 15 references. (Author abstract modified)

002312 Middaugh, Lawrence D.; Zemp, John W. Department of Biochemistry, Medical University of South Carolina, Charleston, SC 29401 **Effects of methadone on activity and on brain monoamines in two strains of mice.** Pharmacology Biochemistry and Behavior. 5(3):367-370, 1976.

Two strains of mice were used to determine the effects of single and multiple injections of methadone on open field activity and on brain monoamines. For the DBA strain, the initial injection of methadone produced an attenuation of locomotor activity. After 7 daily injections, activity increased to that of controls. For the C57 strain, the initial injections produced a slight increase in activity which became more pronounced after further daily injections. Norepinephrine concentration was elevated in brains of DBA mice chronically exposed to methadone. This effect was not observed in C57 mice nor in either strain injected only once with the drug. Serotonin concentration was not altered in animals of either strain whether acutely or chronically exposed to methadone. The results of this study suggest: 1) that activity change following methadone injections is dependent upon genetic factors and previous experience with the drug; 2) that the tolerance develops to the drug produced decreases but not increases in activity; and 3) that chronic exposure to the drug can elevate norepinephrine concentration in brains of DBA mice. 19 references. (Author abstract)

002313 Mikhalenko, I. N.; Kiseleva, I. P.; Lapin, I. P. Leningradskiy nauchno-issledovatel'skiy psikhonevrologicheskiy institut imeni V. M. Bechtereva, Leningrad, USSR /**Absence of an antidepressive effect of lithium in the clinic and in experiments.**/ Otsytstviye antidepressivnogo deystviya litiya v klinike i eksperimente. Zhurnal Nevropatologii i Psikhiatrii Imeni S. S. Korsakova (Moskva). 76(8):1219-1224, 1976.

During long-term treatment of over 200 manic-depressive patients with lithium carbonate, no antidepressant effect was observed. Lithium carbonate in a dose of 1500-1800mg/day was given to 220 patients with manic-depressive psychosis. Of these, 55 were in the depressed phase, 89 were in the manic phase, and 76 were experiencing lucid intervals. No evidence of improvement in the depressive phase was found; in fact, 24 of the 55 depressed patients deteriorated. Studies were performed of the interaction of lithium with reserpinein mice, of the effect of lithium on amphetamine induced motor activity in rats, and of the lack of anantidepressant action of lithium in frogs. It is suggested that the clinical tidepressant effect of lithium observed by some researcher may due to a general tranquilizing action of lithium. 35 references.

002314 Mineyeva-Vyalykh, M. F.; Rayevskiy, K. S. Laboratoriya neyrokhimicheskoy farmakologii Instituta farmakologii AMN SSSR, Moscow, USSR /**Effects of neuroleptics on tyrosine hydroxylase of synaptosomes of the rat hypothalamus.**/ Vliyaniye neyroleptikov na tirozingidroksilazu sinaptosom gipotalamusa krys. Byulleten' Eksperimental'noy Biologii i Meditsiny (Moskva). 81(4):434-436, 1976.

A study was made of the direct effect of various neuroleptics on tyrosine hydroxylase isolated from rat hypothalamic synaptosomes. A direct spectrophotometric method was used, based on measurement of absorbance of 335 nm. At a tyrosine concentration of 0.15 muM haloperidol, haloanisone and fluphenazine increased, and triperidol, droperidol and carbidine decreased the initial rate of tyrosine hydroxylase reaction. The neuroleptics used eliminated substrate inhibition of the enzyme occurring with a rise of tyrosine concentration to 0.3mM. The Michaels constant value for tyrosine failed to change with the action of neuroleptics. It is concluded the effect of neuroleptics may be assumed to be of allosteric nature. 6 references.

002315 Mitchell, S. C.; Waring, R. H. Biochemistry Department, University of Birmingham, Birmingham B15 2TT, England **The metabolism of chlorpromazine in the neonatal guinea-pig.** Xenobiotica (London). 6(12):763-768, 1976.

The metabolism of chlorpromazine in the neonatal guinea-pig was studied. Maximal urinary excretions of sulfoxide occurred at 5 and 14 days, maximum excretion of both conjugated phenols and glucuronides at about 10 and 18 days. It is concluded that metabolite levels in the neonatal guinea-pig show marked variations, values approaching adult levels not being reached before the third week of life. 26 references. (Author abstract modified)

002316 Mollenauer, Sandra; Plotnik, Rod; Bean, N. Jay. San Diego State University, San Diego, CA 92182 **Effects of scopolamine on smell discrimination in the rat.** Physiological Psychology. 4(3):357-360, 1976.

The effects of scopolamine on smell discrimination in the rat were studied to determine if scopolamine caused a general blockade of olfactory perception. Rats were trained to perform a smell discrimination and head poke response for food reinforcement. Following treatment with saline or scopolamine (SCO), rats were retested on these two tasks as well as on passive avoidance. Scopolamine significantly impaired passive avoidance and head poke responding. Scopolamine also caused a delay in the onset of discrimination performance. The results of the smell discrimination test indicate that scopolamine did not cause a complete blockade of olfactory perception. The results of the head poke test suggest that scopolamine might increase vibrissae sensitivity. 8 references. (Author abstract modified)

002317 Morgan, B. A.; Smith, C. F. C.; Waterfield, Angela A.; Hughes, J.; Kosterlitz, H. W. Pharmaceutical Division, Reckitt & Colman, Hull, HU8 7DS, England **Structure-activity relationships of methionine-enkephalin.** Journal of Pharmacy and Pharmacology (London). 28(8):660-661, 1976.

An overview of research on the amino acid structural activity relationships of methionine/enkephalin and opiate receptors in brain homogenates and other tissues of various addicted animals is presented. It is posited that an amino acid with a hydrophobic side-chain at the C-terminus and intact tyrosine residue at the N-terminus is essential for activity of the pentapeptide. It was concluded that: 1) modification at either the N-terminus or the C-terminus would lead to major loss of activity of methionine/enkephalin; and 2) this biological lability makes methionine/enkephalin good candidates for the role of neurotransmitters or neuromodulators. 13 references.

002318 Nagai, Kazuo; Iwaki, Yo. Department of Pharmacology, Hyogo College of Medicine, Hyogo 663, Japan **Nicotine convulsion and brain dopamine contents in rats and mice after long term administration of Li2CO3.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):102P, 1976.

At the 49th annual meeting of the Japanese Pharmacological Society, Osaka, Japan, in March 1976, a study of the relationship between nicotine convulsions and brain dopamine contents in rats and mice after long-term administration of lithium carbonate (LiC) was reported. The concentrations of lithium (Li), sodium (Na), potassium (K), calcium (Ca) and catecholamines in plasma and brain were measured after long-term drinking of LiC. Ca levels were higher in experimental than control animals. Na and K levels in plasma were not changed but Ca levels were increased. Nicotine induced tremor clonic convulsions, and tonic convulsions were delayed by LiC. The convulsive dose of nicotine was increased by LiC. The whole brain dopamine content was decreased after nicotine induced clonic convulsions but the ratio of decreased dopamine was lower in the animals on LiC. It is suggested that dopamine may play a role in the production of nicotine convulsions and that the balance of cations in the brain, especially Ca, may also participate in this effect. (Author abstract modified)

002319 Nakagawa, Kazuo; Kuriyama, Kinya. Department of Pharmacology, Kyoto Prefectural University of Medicine, Kyoto 602, Japan **Morphine-induced changes of cyclic AMP metabolism and protein kinase activity in brain.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):110P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March 1976, a study of the effect of morphine administration on cyclic narcotic analgesic, opiate metabolism and cyclic AMP dependent protein kinase activity of mouse cerebral cortex was reported. Acute oral administration of morphine had no significant effect on the activities of adenylate cyclase, phosphodiesterase and cyclic AMP protein kinase or on the formation of 14C-cyclic AMP in slices prelabelled with 14C-adenine. Morphine administration by the implantation method induced a slight increase in the activity of cyclic AMP protein kinase in the cruce mitochondrial (P2) fraction, whereas that in the microsomal (P3) fraction as well as the activity of adenylate cyclase of P2 was reduced. Continuous oral administration of morphine induced an increase in activities of both adenylate cyclase and cyclic AMP protein kinase in the P2 fraction. Normal levels were reverted to within 7 to 10 da after the withdrawal of morphine. By subfractionating the P2 the increment observed in the activity of cyclic AMP protein kinase following continuous oral administration of morphine was found to mainly due to increase in the activity of synaptosomal enzyme. The results suggest that continuous oral administration of morphine induces the activation of activities of adenylate cyclase as well as cyclic AMP dependent protein kinase of synaptosomes and that these changes may be involved in the development and/or maintenance of alterations of central nervous system functions associated with morphine dependence and/or tolerance. (Author abstract modified)

002320 Nakamura, Kazuo; Nakamura, Keiji. Department of Pharmacology, Nippon Roche Research Center, Kamakura 247, Japan. **Interaction of benzodiazepine drugs with striatal dopaminergic neurons in the brain.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):101P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March 1976, a study of the effects of benzodiazepines on dopamine (DA) containing neurons in the cerebral regions of the rat was reported. Diazepam and clonazepam significantly decreased the levels of the DA metabolites homovanillic acid (HVA) and dihydroxyphenylacetic acid (DOPAC) in the striatum and the concentration of DOPAC in the cortex but not in the mesolimbic olfactory tubercle, septum or hypothalamus. Clonazepam slightly but significantly enhanced the stereotyped behavior induced by the DA agonists apomorphine and dextro-methamphetamine. Investigation of the influence of clonazepam on the in vitro DA sensitive adenyl cyclase system in homogenates of striatum and cortex revealed that the drug does not change the cyclic adenosine monophosphate (AMP) generating system. When combined with various doses of DA, clonazepam significantly increased the DA accumulation of cyclic AMP in the striatum but not in the cortex. It is suggested that the decreased DOPAC and HVA concentrations in the striatum and stimulation of DA agonist induced stereotyped behavior observed after benzodiazepine administration were due to reflex of the indirect stimulation of postjunctional DA neurons, and that the indirect, postjunctional stimulation of striatal DA neurons is at least partly involved in the anticonvulsant and tranquilizing effects of clonazepam. (Author abstract modified)

002321 Naumov, Yu. I.; Ivkov, N. N.; Matyushin, A. I. 2 Moskovskiy meditsinskiy institut im. N. N. Pirogova, Moscow, USSR /**Oxidative phosphorylation in various parts of the rat brain following morphine administration.**/ Okislitel'noye fosforilirovaniye razlichnykh otdelov golovnogo mozga krys pri vvedenii morfina. Farmakologiya i Toksikologiya (Moskva). 39(6):662-665, 1976.

The effects of morphine introduced intraperitoneally and in vitro on oxidative phosphorylation of the brain cortex and brainstem was studied in rats. Morphine i.p. intensified the rate of substrate oxidation. During the first days of administration the narcotic analgesic inhibited oxidation of mitochondria released from the brainstem, and once narcotic habituation had developed, the inhibition ceased to be effective. The phosphorylation effect remained unchanged in the in vivo and in vitro experiments. The data suggest that with developing habituation to morphine the functions of brainstem and brain cortex mitochondria do not undergo any substantial change. 3 references. (Journal abstract modified)

002322 no author. no address /**How tranquilizers act on the brain.**/ Comment les tranquillisants agissent-ils sur le cerveau? Recherche (Paris). 7(71):858, 1976.

The mode of action of minor tranquilizers on the brain is discussed. A number of psychoactive substances capable of

modifying mental activity produce their effects by interference with the chemical mediation of nerve transmission at the level of the interneuronal synapses. For the psychotropic substances best known by the general public, namely chlordiazepoxide and diazepam, a mechanism of this type has not yet been found. However, in an in vitro culture of Purkinje cells from the cerebellum, chlordiazepoxide and diazepam have been shown to be capable, in weak doses, of noticeably accelerating the spontaneous electrical activity of these cells. The neuromediator gamma-aminobutyric acid (GABA) slows this activity. Thus, diazepam and chlordiazepoxide seem to act as antagonists of the synaptic mediation by GABA, at least at the level of the cells of the cerebellum. 4 references.

002323 Noravyan, O. S.; Avakyan, O. M. Institut tonkoy organicheskoy khimimii im. A. L. Mndzhoyana, AN Arm. SSR, Yerevan, USSR **/Action of practolol and propranolol on the effects of isadrine in laboratory animals./** Deystviye praktolola i propranolola na effekty izadrina u laboratornykh zhivotnykh. Zhurnal Eksperimental'noy i Klinicheskoy Meditsiny (Yerevan). 16(3):8-14, 1976.

The influence of i.v. practolol and propranaolol on the effects of i.v. isadrine was studied in 70 rats, 14 rabbits, 18 cats and 10 dogs. It was determined that under identical experimental conditions the beta-adrenoblocking action of practolol and propranolol disappears rapidly in rats, but continues for a relatively long time in cats and dogs. It is concluded that experiments on rats may be used to judge the intensity and duration of beta-adrenoblocking action. 17 references. (Author abstract modified)

002324 Oguri, Kazuta; Lee, Nancy M.; Loh, Horace H. Faculty of Pharmaceutical Sciences, Kyushu University, Fukuoka, Japan **Apparent protein kinase activity in oligodendroglial chromatin after chronic morphine treatment.** Biochemical Pharmacology (Oxford). 25(21):2371-2376, 1976.

Cyclic adenosine monophosphate (cyclic AMP) independent phosphorylation of nonhistone protein in oligodendrogial chromatin was studied using material purified from the oligodendroglial nuclei of mice after chronic morphine treatment. Morphine sulfate in vitro had no effect on phosphorylation. However, chronic morphine treatment resulted in an increase of phosphorylation in high molecular weight regions of sodium dodecylsufate electrophoresis gel. It is suggested that the increase in phosphorylation is due to protein kinase activity rather than to a decrease of phosphoprotein phosphatase activity. 15 references. (Author abstract modified)

002325 Ohta, Masahiro. Department of Physiology, Faculty of Medicine, Kyushu University, Fukuoka 812, Japan **Haloperidol blocks an alpha adrenergic receptor in the reticulocortical inhibitory input.** Physiology & Behavior. 16(4):505-507, 1976.

The blocking effect of haloperidol in reticulocortical inhibition was examined in rats. The reticular inhibition of I waves of the pyramidal tract response was significantly reduced by haloperidol, applied topically to the cortical surface, at a higher concentration than that used to block dopamine receptors preferentially. The blocking activity of haloperidol was much weaker than that of the alpha adrenergic blockers phentolamine or phenoxybenzamine. The reticulocortical facilitation was unaffected by any of these agents. The results suggest that the reticulocortical inhibition may be mmediated by noradrenaline and that the receptor sites are distributed in the cerebral cortex. 15 references. (Author abstract)

002326 Ohuchi, Takeshi; Tanaka, Shozo; Takenaka, Fumio. First Department of Pharmacology, Kumamoto University, Medical School, Kumamoto 860, Japan **Serum dopamine-beta-hydroxylase activity (V): effects of various drugs on the enzyme activity.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):49P, 1976.

At the 49 general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study of the effects of various pharmacological agents on serum dopamine-beta-hydroxylase (s-DBH) activity was reported. Norepinephrine, methoxamine and phenylephrine decreased s-DBH level presumable through the mechanism of alpha-adrenergic inhibition effect catecholamine (CA) release. Amphetamine and methamphetamine produced enhanced release of CAs and increased s-DBH activity after a single injection. Dopamine, when infused into the vein, produced a gradual rise in s-DBH activity together with an elevation of the blood pressure; normal levels were reverted to within 10 min after a discontinuance of the infusion. Angiotensin II markedly lowered s-DBH activity during the course of infusion. Reserpine showed biphasic actions on s-DBH activity (i.e.,an initial rise followed by a long lasting fall in s-DBH activity). After a single injection of reserpine, tyramine had little effect on blood pressure and a decreased effect on s-DBH level. Partial restoration of the pressor effect of tyramine by an infusion of norepinephrine failed to restore the effect on s-DBH activity. (Author abstract modified)

002327 Osnyach, V. S.; Kudrin, V. S.; Matyushin, A. I. Vtoroy Moskovskiy meditsinskiy institut im. N. I. Pirogova, Moscow, USSR **Investigation of the effect of narcotic analgesics (phenanthrene derivatives) on physical chemical properties of nucleic acids./** Issledovaniye deystviya narkoticheskikh anal'getikov (proizvodnykh fenantrena) na fiziko-khimicheskiye svoystva nukleinovykh kislot. Farmakologiya i Toksikologiya (Moskva). 39(5):549-552, 1976.

An attempt was made to establish, in experiments in vitro, the nature of possible changes in the structure of the DNA molecule in the presence of various agents of the morphine group. DNA taken from rat liver was combined with pharmacological preparations by heat denaturation. Viscosimetry, enzyme activity, and radioisotope analysis were checked by computer. Morphine and its analogs were found either to not affect (or only weakly affect) the basic traits of DNA, and their effects on cell metabolism do not appear to be linked with their interaction with DNA or its components. 6 references.

002328 Paden, Charles; Wilson, Charles J.; Groves, Philip M. Department of Psychology, University of Colorado, Boulder, CO 80309 **Amphetamine-induced release of dopamine from the substantia nigra in vitro.** Life Sciences (Oxford). 19(10):1499-1506, 1976.

To test the hypothesis that amphetamine releases dopamine from the substantia nigra in vitro, chopped rat brain tissues from the substantia nigra were incubated in a d-amphetamine solution and amphetamine induced dopamine release was assessed. Analysis of data indicated a significant release of (3H)dopamine into the incubation medium. This effect was observed with both exogenous (3H)dopamine previously taken up by the tissue and (3H)dopamine endogenously synthesized from L-(3,5-3H)tyrosine. The observed release was greater in magnitude when the apparent conversion of released dopamine to 3-methoxytyramine was taken into account. The relevance of the present results to the previously postulated self-inhibition by dopaminergic neurons of the substantia nigra pars

compacta is discussed. The present data also provide support for the concept that cathechol-O-methyltransferase is located primarily extraneuronally in brain. 31 references. (Author abstract modified)

002329 Page, J. G.; Sullivan, H. R.; Due, S. L. Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, IN 46206 **Metabolism of 1,4 dihydro 6 trifluoromethylquinoxaline 2,3-dione (Lilly 72525) in rats and cats.** Xenobiotica (London). 6(12):713-723, 1976.

The metabolism of 1,4-dihydro-6-trifluoromethylquinoxaline-2,3-dione (Lilly 72525), a sedative hypnotic drug, was studied in rat and cat. Plasma concentrations of Lilly 72525 were measured fluorometrically after oral and intravenous doses of the compound in rats. A comparison of the area under the two curves suggested that 84% of the oral dose was absorbed. Studies with 14C-labeled material in both species confirmed that the drug was well absorbed after oral administration and revealed that the dione was mainly eliminated unchanged in the urine. Bile duct cannulation experiments suggested that biliary excretion accounted for most or all of the drug present in feces of rats. Metabolites isolated from urinary extracts were identified by gas/liquid chromatography -- mass spectrometry. The only metabolite detected in rat urine or bile extracts was a ring hydroxylated compound. This metabolite plus two N-hydroxylated metabolites were identified in extracts of cat urine. 6 references. (Author abstract)

002330 Patel, Mulchand S.; Owen, Oliver E.; Raefsky, Cindy. Dept. of Medicine, General Clinical Research Center, Temple Univ. School of Medicine, Philadelphia, PA 19140 **Effect of methylmalonate on ketone body metabolism in developing rat brain.** Life Sciences. 19(1):41-47, 1976.

The effects of methylmalonate on the metabolism of ketone bodies in developing rat brain were studied in vivo and in vitro. The oxidation of radiolabeled 3-hydroxybutyrate to carbon dioxide and its incorporation into cerebral lipids by cortex slices from 1 week old rats were markedly inhibited by methylmalonate. Methylmalonate had no effect on the metabolism of labelled acetoacetate, glucose, and acetate by brain slices. Addition of propionate in the incubation medium reduced cerebral lipogenesis from labeled 3-hydroxbutyrate and acetate. Acute methylmalonic acidemia induced in 1 week old pups by injecting 3% methylmalonate solution caused a reduction in the incorporation of labeled 3-hydroxybutyrate into cerebral lipids. However, acute methylmalonic acidemia had no effect on cerebral lipogensis in vivo from labeled acetate. These findings show that the conversion of 3-hydroxybutyrate to acetoacetate by 3-hydroxybutyrate dehydrogenase in the brain is inhibited by methylmalonate, and that propionate, which also accumulates in patients with methylmalonic aciduria, inhibits cerebral lipid synthesis. 23 referen es. (Author abstract modified)

002331 Patkina, N. A.; Lapin, I. P. Leningradskiy NI psikhonevrologicheskiy institut im. V. M. Bekhtereva, Leningrad, USSR /**Study of monoaminergic mechanisms of haloperidol action in experiments with cats.**/ Izucheniye monoaminergicheskikh mekhanismov deystviya galoperidola, v opytakh na koshkakh. Farmakologiya i Toksikologiya (Moskva). 39(5):520-524, 1976.

The comparative roles of different monoamines in the action of haloperidol were investigated in experiments on 22 male cats with electrodes implanted in the hypothalamus, using a reward and punishment model. Haloperidol was used against a background of dopaminomimetic amantadine and precursors of the biogenic amines L-DOPA, tryptophan, and 5-OTP. The inhibitive effect of haloperidol on reward systems was found to occur at the expense of its serotonin negative effect. Haloperidol participated in stimulus of the punishment system through its serotonin and dopamine negative effects. 8 references. (Author abstract modified)

002332 Pearl, Ronald G.; Seiden, Lewis S. no address **The existence of tolerance to and cross-tolerance between d-amphetamine and methylphenidate for their effects on milk consumption and on differential reinforcement of low rate performance in the rat.** Journal of Pharmacology and Experimental Therapeutics. 198(3):635-647, 1976.

The effects of dextroamphetamine and methylphenidate on milk consumption, operant behavior, and brain levels of norepinephrine (NE) were studied in rats. Both dextroamphetamine and methylphenidate decreased milk consumption and both drugs produced similar disruptions in responding under differential reinforcement of low rate (DRL) contingencies. Tolerance to these effects occurred with daily administration, and cross-tolerance between dextroamphetamine and methylphenidate also occurred. Daily administration of dextroamphetamine, but not of methylphenidate, resulted in decreased NE levels in the brain. The reduction in NE levels is believed to result from the storage in noradrenergic neurons of parahydroxynorephedrine, a metabolite of dextroamphetamine. No radioactivity was detected in the brain after daily doses of radiolabeled methylphenidate, suggesting that only dextroamphetamine is metabolized to a compound which is stored in noradrenergic neurons. The existence of behavioral cross-tolerance between dextroamphetamine and methylphenidate is therefore inconsistent with the hypothesis that tolerance to the behavioral effects of dextroamphetamine is due to the metabolism of dextroamphetamine to parahydroxynorephedrine, a false transmitter in noradrenergic neurons. 58 references. (Author abstract modified)

002333 Peck, Ernest J., Jr.; Miller, Ann L.; Lester, Bruce R. Baylor College of Medicine, Houston, TX 77030 **Pentobarbital and synaptic high-affinity receptive sites for gamma-aminobutyric acid.** Brain Research Bulletin. 1(6):595-597, 1976.

The effect of pentobarbital on the high affinity uptake and binding of gamma-aminobutyric acid (GABA) to synaptic receptive sites was examined in order to determine whether the previously reported effect of pentobarbital (enhancement of the inhibitory actions of GABA via amplification and prolongation of receptor activation) is mediated at presynaptic or postsynaptic sites. Using synaptosomes and subsynaptosomal fractions of cerebral cortex and hippocampus, it was found that concentrations of pentobarbital which exert a synaptic influence in electrophysiological experiments have no appreciable effect on GABA uptake or binding. It is concluded that the effect of pentobarbital is mediated by mechanisms other than the high affinity uptake or binding of GABA. Possible sites of action include the presynaptic release of GABA and the ionophores coupled with postsynaptic sites. 12 references. (Author abstract modified)

002334 Pert, Agu; Walter, Marc. Adult Psychiatry Branch, National Institute of Mental Health, Bethesda, MD 20014 **Comparison between naloxone reversal of morphine and electrical stimulation induced analgesia in the rat mesencephalon.** Life Sciences (Oxford). 19(7):1023-1032, 1976.

Comparisons were made between the efficacy of naloxone in rats to reverse analgesia induced by electrical stimulation

(SPA) of the periaqueductal gray matter, and analgesia induced by microinjections of morphine into the same brain region. Naloxone at 1mg/kg or 10mg/kg was ineffective in antagonizing SPA during the first 2 minutes poststimulation. Some antagonism did appear 3 to 5 min after stimulation, but the effect was neither consistent nor dose dependent. Morphine, on the other hand, was antagonized completely in a dose dependent response by naloxone. The assumption that similar mechanisms underlie both opiate and electrical stimulation induced analgesia does not appear to be demonstrated. 35 references. (Author abstract)

002335 Pert, Candace B.; Gulley, Blynn L. Adult Psychiatry Branch, NIMH, 9000 Rockville Pike, Bethesda, MD 20014 **The mechanism of opiate agonist and antagonist action. (Unpublished paper).** Bethesda, MD, NIMH, 1976. 29 p.

In vivo and in vitro studies elucidating mechanisms of opiate agonist and antagonist action are reviewed and implications for future research are discussed. Research indicating the existence of specific opiate binding is reviewed. Research with naloxone and other opiate antagonists suggest agonist/antagonist competition at the same receptors. Comparison of opiate agonist/antagonist pairs indicated that antagonist binding is facilitated by sodium while agonist binding is inhibited. Further research into the sodium shift has shown that rather than there existing two distinct agonist and antagonist groups of opiates, there exists rather a continuous spectrum between these two poles and that opiates possess two distinct dimensions: the apparent affinity for the receptor in the presence of sodium; and the relative agonist/antagonist property of the drug as determined by the ratio of the apparent affinity in the absence and presence of sodium. The biochemical basis of the sodium effect is considered. Recent research into endogenous opiate receptor ligands and the neurotransmitter hypothesis is reviewed. Future research on the physiological and evolutionary significance of this dual endogenous opiate system is suggested. 72 references.

002336 Phillis, J. W.; Edstrom, J. P. Department of Physiology, College of Medicine, University of Saskatchewan, Saskatoon, Canada **Effects of adenosine analogs on rat cerebral cortical neurons.** Life Sciences (Oxford). 19(7):1041-1053, 1976.

The effects of adenosine analogs on rat cerebral cortical neurons were studied. Adenosine analogs, adenosine transport blockers, and adenosine deaminase inhibitors were used to examine the nature of the adenosine receptor and possible routes of metabolism of extracellularly released adenosine. 2-Halogenated derivatives of adenosine were potent depressors of cortical neuron firing rate, while 2-aminoadenosine and 2-hydroxyadenosine were slightly less potent depressors than adenosine. The alpha-beta-methylene isosteres of 5′-adenosine diphosphate (5′-ADP) and 5′-adensine triphosphate (5′-ATP) were almost devoid of agonist activity, while the beta-gamma-methylene analog was an active agonist. It is suggested that ADP and ATP may be converted to adenosine monophosphate (AMP) or possibly adenosine before they can activate the adenosine receptor; 2, 3, and 5′-deoxyadenosine depressed spontaneous firing without antagonizing the effect of adenosine. Adenosine deaminase inhibitors, deoxycoformycin and erythro-9-(2-hydroxy-3-nonyl)adenine had potent, long-lasting depressant actions on the spontaneous firing of cortical neurons and concurrently potentiated the actions of adenosine or 5′-AMP. Inhibitors of adenosine transport, papaverine and 2-hydroxy-5-nitrobenzylthioguanosine, prolonged the duration of action of adenosine and 5′-AMP. Intracellular recordings show that 5′-AMP hyperpolarizes cerebral cortical neurons and suppresses spontaneous and evoked excitatory postsynaptic potentials, in the absence of any pronounced alterations in membrane resistance. 25 references. (Author abstract modified)

002337 Pieri, L.; Haefely, W. Pharmaceutical Research Dept., F. Hoffman-La Roche & Co., Grenzacherstr., 124, CH-4002, Basel **The effect of diphenylhydantoin, diazepam and clonazepam on the activity of Purkinje cells in the rat cerebellum.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 296(1):1-4, 1976.

To investigate the effects of dyphenlyhydantoin, diazepam, and clonazepam on the activity of Purkinje cells, unanesthetized curarized male rats were intravenously injected with these drugs, and spike discharges of single cerebellar Purkinje cells were recorded continuously with extracellular microelectrodes. Diphenylhydantoin in doses between 10 and 100mg/Kg did not substantially alter the activity of Purkinje cells within 2 to 3 h. The two benzodiazepines, diazepam, and clonazepam, already in low intravenous doses (0.03-0.1mg kg-1) consistently and reversibly depressed the firing rate. The results do not support the previously advanced hypothesis that these drugs reduce epilepti-form activities by increasing the output from the cerebellar cortex. They rather point to the possibility that a reduced firing rate of cerebellar Purkinje cells mediates at least in part ataxia and muscular hypotonia observed after these drugs. 21 references. (Author abstract)

002338 Plenge, P.; Mellerup, E. T. Psychomemistry Institute, Rigshospitalet, 9, Blegdamsvej, DK-2100 Copenhagen, Denmark **Lithium effects on serum calcium, magnesium and phosphate, in rats.** Psychopharmacology (Berlin). 49(2):187-190, 1976.

The effects of lithium on serum calcium, magnesium, and phosphate was studied in control rats and in rats after removal of the parathyroid glands (PTX) or removal of both thyroid and parathyroid (TX-PTX) glands. Serum calcium was unaffected by lithium in unoperated and in PTX rats but was increased by lithium in the TX-PTX rats. Serum magnesium was increased and serum phosphate was slightly decreased by lithium in all three groups. It is concluded that lithium increases both serum calcium and serum magnesium, but in the intact animal only a slight increase or no increase in serum calcium is seen after lithium due to physiological control mechanisms. After removal of the calcitonin producing cells in the thyroid gland the animal is unable to produce a fast decrease in serum calcium and lithium is then able to increase the serum calcium concentration. 19 references. (Author abstract modified)

002339 Plenge, Per. Psychochemistry Institute, Rigshospitalet, 9, Blegdamsvej, DK-2100 Copenhagen, Denmark **Acute Lithium affects on rat brain glucose metabolism -- in vivo.** International Pharmacopsychiatry (Basel). 11(2):84-92, 1976.

Administration of LiCl to rats was found to affect brain glucose metabolism. The concentrations of brain glucose, brain lactate and brain glycogen were increased and the concentration of brain glutamate was decreased. Results were explained by a lithium induced increase in brain uptake and an increased rate of glysolysis, and a slight inhibition of the oxidative decarboxylation of the Krebs cycle. It is concluded that lithium inhibits a step in either the oxidative decarboxylation of pyruvate or a step associated with the Krebs cycle. 14 references. (Author abstract modified)

002340 Poddubiuk, Zbigniew M.; Kleinrok, Zdzislaw. Department of Pharmacology, School of Medicine, Jaczewskiego 8,

20-090 Lublin, Poland **A comparison of the central actions of prostaglandins A1, E1, E2, F1alpha, and F2alpha in the rat: II. The effect of intraventricular prostaglandins on the action of some drugs and on the level and turnover of biogenic amines in the rat brain.** Psychopharmacology (Berlin). 50(1):95-102, 1976.

The effects of intraventricular prostaglandins (PGs) on the sleep inducing action of hexobarbital, chloralhydrate, and ethanol, and on the level and turnover of biogenic amines in the rat brain were examined. PGs injected into the right lateral ventricle of the rat increased the sleeping time induced by these drugs. PGE1 and PGE2 intensified chlorpromazine induced catalepsy, inhibited amphetamine hyperactivity, and significantly depressed the amphetamine induced stereotypy. Noradrenaline concentrations were decreased by PGE1 and PGE2 and were increased by PGF2alpha. PGF2alpha increased both serotonin and 5-hydroxyindoleacetic acid levels in rat brain. Total acetylcholine concentrations were increased by PGF1alpha and PGF2alpha. PGE1, PGE2, and PGF2alpha enhanced the turnover of dopamine, noradrenaline, and serotonin. PGE2 counteracted the decreased activity induced by alpha-methyltyrosine and abolished the hypothermic action of alpha-methyltyrosine. PGF2alpha had little effect on the activity of para-chlorophenylalanine pretreated rats, whereas the higher doses of PGF2alpha increased body temperature in these animals. 38 references. (Author abstract)

002341 Popova, E. N.; Smol'nikova, N. M.; Strekalova, S. N.; Frumkina, L. Ye. Institut mozga AMN SSSR, Moscow, USSR **/Structural changes in caudate nucleus in the progeny of rats subjected to the action of chlorpromazine./** Strukturnye izmeneniya neyronov khvostatogo yadra u potomstva krys, podvergavshikhsya vozdeystviyu aminazina. Farmakologiya i Toksikologiya (Moskva). 39(6):645-647, 1976.

Because previous studies have shown that administration of chlorpromazine to pregnant rats resulted in heightened spontaneous motor activity of offspring, a study was undertaken of the effect of chlorpromazine on caudate nucleus neurons of the progeny. Results showed administration of chlorpromazine throughout pregnancy produced accelerated maturation of caudate nucleus neurons in the test offspring, with more complete neuron structure and greater dendrite formation. The data obtained are in accord with physiological observations in test rats compared to control individuals. 14 references.

002342 Premont, J.; Tassin, J. P.; Thierry, A. M.; Bockaert, J. Laboratoire de Physiologie Cellulaire, College de France, F-75231 Paris Cedex 05, France **Repartition and drug sensitivity of dopamine and L-isoproterenol-sensitive adenylate cyclases in rat brain homogenates.** Advances in Biochemical Psychopharmacology. 15:347-356, 1976.

A method that permits the measurement of adenylate cyclase activity in homogenates of single disc thickness is described, and results of studies in which the technique was used to investigate the characteristics of dopamine (DA), l-isoproterenol, and d-lysergic acid diethylamide (LSD) stimulated adenylate cyclases are reported. In rat striatum, DA stimulated adenylate cyclase activity by 3.5fold. This effect was completely blocked by fluphenazine and by phentolamine. LSD stimulated the adenylate cyclase activity by interacting with DA receptors, producing a 1.4fold maximal increase. Isoproterenol activated adenylate cyclase present in rat striatum homogenates through a receptor distinct from the DA receptor; this stimulation was not affected by fluphenazine or phentolamine but was suppressed by racemic propranolol. The topographical distributions of DA stimulated adenylate cyclase activity and endogenous DA content were also examined in homogenates of striatum. A 4.8fold progressive decrease in the amount of cyclic adenosine monophosphate (cAMP) produced in the presence of DA was observed from the rostral to the caudal part of the structure. The LSD sensitive adenylate cyclase followed a similar distribution. The topographic distribution of endogenous DA was comparable to the distribution of the DA sensitive adenylate cyclase, suggesting that this enzyme is an integral part of the DA synapses. It was also found that the frontal cortex contains a DA sensitive adenylate cyclase. 24 references.

002343 Psatta, Dan M. Institute of Neurology and Psychiatry, Academy of Medical Sciences, Bucharest, Romania **The effects of some drugs (eserine, atropine, reserpine, niamid) upon the EEG manifestations of experimental neurosis in adult cats.** Neurologie et Psychiatrie (Bucuresti). 14(4):283-293, 1976.

A model of experimental neurosis was tested in which adult cats having neurosis were given the four psychotropic drugs eserine, atropine, reserpine, and niamid in order to observe their correlative effect of EEG and behavioral manifestations of neurosis. Administration of drugs acting upon the cholinoreactive and adrenoreactive systems prove the inhibitory neurosis to be ergotropic and not trophotropic in origin. Esterine induced disappearance of slow rhythms from the neocortex, reappearance of hippocampal theta activity and improvement in STM (delayed approach avoidance alternation) but failed to abolish neurosis which only changed from the inhibitory to the excitatory type. Atropine had no effect in small doses; at higher dosages it abolished pathological memory traces as well as any other aftereffect of preparatory stimuli and showed antiphobic properties. Reserpine induced replacement of abnormally fast rhythms by theta rhythms in the hippocampus, occurrence of slow rhythms in the posterior hypothalamus and antidepressant effects; behavioral exhaustion phenomena occurred on high dosages only. Niamid reversed the effects of reserpine and worsened the manifestations of inhibitory neurosis (catatonia, hippocampal fast rhythms, neocortical slow waves). The somewhat unexpected behavioral effects of these drugs in neurotic animals are discussed in relation to their EEG effects during trials of successive approach/avoidance differentiation and which show that inhibitory neurosis is ergotropic and not trophotropic in origin, as previously suggested. 15 references. (Author abstract modified)

002344 Rebec, George V.; Groves, Philip M. Department of Psychiatry, School of Medicine, University of California at San Diego, La Jolla, CA 92093 **Enhancement of effects of dopaminergic agonists on neuronal activity in the caudate-putamen of the rat following long-term d-amphetamine administration.** Pharmacology Biochemistry and Behavior. 5(3):349-357, 1976.

The effects of the dopaminergic agonists dextroamphetamine and apomorphine on the firing rates of neurons in the caudate/putamen of rats were examined in animals pretreated with amphetamine and in controls. In the saline pretreated controls, dextroamphetamine produced an initial, brief potentiation of neuronal firing that was followed by a marked depression of neuronal activity lasting for 35 min to 110 min after injection. In amphetamine pretreated animals, the depression of neuronal activity produced by the same dose of amphetamine was markedly prolonged. A similar effect occurred in response to apomorphine in amphetamine pretreated animals. The results are discussed in relation to the known behavioral and biochemical effects of acute and long term amphetamine administration. 37 references. (Author abstract modified)

002345 Reinhard, John F. Jr.,; Kosersky, Donald S.; Peterson, George R. Laboratory of Neuroendocrine Regulation, Dept. of Nutrition and Food Science, MIT, Cambridge, MA 02139 **Strain-dependent differences in responses to chronic administration of morphine: lack of relationship to brain catecholamine levels in** Life Sciences (Oxford). 19(9):1413-1420, 1976.

The strain dependent differences in responses to chronic administration of morphine and the lack of relationship to brain catecholamine levels was studied in mice. When measured for weight loss, mortality and degree of physical dependence, four strains of mice exhibited widely differing sensitivities to chronically administered morphine. No obvious relationship existed between the pharmacological responses to morphine and the steady state levels of either norepinephrine or dopamine in brain striatal sections of the strains tested. It is concluded that the naloxone precipitated withdrawal jumping response may not be associated with an elevation of brain dopamine levels. 23 references. (Author abstract modified)

002346 Rivera-Calimlim, Leonor. Pharmacology and Toxicology, University of Rochester, School of Medicine and Dentistry, Rochester, NY 14642 **Effect of lithium on gastric emptying and absorption of oral chlorpromazine.** Psychopharmacology Communications. 2(3):263-272, 1976.

It has been suggested that low plasma levels of chlorpromazine (CPZ) were achieved by patients concurrently taking lithium, despite ingestion of doses of CPZ which ordinarily produce plasma levels of 100 to 300ng/ml or more. This lithium chlorpromazine interaction has been studied in rats. The plasma and brain levels of CPZ after an oral dose were significantly lower in rats treated with lithium, whereas the percent of dose remaining in the stomach (24% to 30%) was significantly higher than in matched controls. Gastric emptying was measured by 14C polyethylene glycol and was shown to be inhibited significantly by oral and i.p. lithium. This inhibition of gastric emptying by lithium may be the major cause of the lower plasma levels of CPZ since diminution of plasma drug levels has been shown for L-dopa, chlorpromazine, sulfa drugs, and phenylbutazone in animals and man treated concomitantly with anticholinergics, which also diminish gastric motility. 13 references. (Author abstract)

002347 Robinson, Susan E.; Sulser, Fridolin. Vanderbilt University School of Medicine, Nashville, TN 37232 **The noradrenergic cyclic AMP generating system in the rat limbic forebrain and its stereospecificity for butaclamol.** Journal of Pharmacy and Pharmacology (London). 28(8):645-646, 1976.

The action of the two enantiomers of butaclamol, a neuroleptic drug, on the specific noradrenaline sensitive cyclic-AMP system in slices of the limbic forebrain of rats is discussed. Results indicate that the blocking effect of butaclamol also resides in the (+) enantiomer, thus demonstrating stereospecificity for central noradrenaline receptor blockade. Although the stereospecific blockade by butaclamol of limbic dopamine receptors is quantitatively more pronounced, the results support the view that blockade of noradrenergic receptors in the limbic system may contribute to the pharmacologic and perhaps therapeutic action of antipsychotic drugs. 13 references.

002348 Rodgers, R. J.; Semple, J. M.; Cooper, S. J.; Brown, K. Department of Psychology, Queen's University of Belfast, Belfast, Northern Ireland **Shock-induced aggression and pain sensitivity in the rat: catecholamine involvement in the corticomedial amygdala.** Aggressive Behavior. 2(3):193-204, 1976.

The possible role of amygdaloid catecholamines in the control of shock induced aggression and pain sensitivity in the rat was investigated. Bilateral microinjections of chlorpromazine into the corticomedial amygdala resulted in decreased fighting and decreased sensitivity to the shock stimulus. Further analysis of this effect, using specific adrenergic antagonists, revealed that neither alpha nor beta-adrenergic systems appeared to be responsible for the behavioral effect of chlorpromazine. Injections of haloperidol into the same region, however, yielded a reduction similar to that produced by chlorpromazine, while dopamine injections resulted in significant elevations in both fighting and pain sensitivity. No effect on any of these behavioral measures was obtained following injection of any of the agents into the basolateral amygdala. These results suggest that the observed effect of catecholamine injections in the corticomedial amygdala is related to changes in pain sensitivity mediated by dopamine. 21 references. (Journal abstract)

002349 Roshchina, L. F. Vsesoyuznyy NII im. S. Ordzhonikidze, Moscow, USSR **/Electroencephalographic analysis of the central effect of pirasidol./** Elektroentsefalograficheskiy analiz tsentral'nogo deystviya pirazidola. Farmalogiya i Toksikologiya (Moskva). 39(4):397-402, 1976.

The effect of pirasidol on bioelectric activity of the brain was studied in 40 cats and 50 rabbits. EEG measurements were taken of the sensorimotor, visual, and parietal regions of the brain in the cats, and in the rabbits, of the reticular formation of the mesencephalon, dorsal hippocampus, and basal nucleus of the amygdala, as well. The results show that pirasidol has an activating effect on EEG indices of the cortex, hippocampus, and reticular formation of the mesencephalon; it shows central adrenaline and serotonin positive action, and intensifies the EEG effect of phenamine, L-dopa, and 5 oxytryptophan. It did not display cholinolytic activity and did not influence electrophysiological effects of anticholinesterase agents or arecoline. 26 references.

002350 Saad, Samir F. Department of Pharmacology, Faculty of Pharmacy, Cairo University, Cairo, Egypt **The effect of certain parasympathomimetic and parasympatholytic drugs on the gamma-aminobutyric acid content in the cerebral hemispheres of mice.** Materia Medica Polona (Warsaw). 8(4):397-399, 1976.

The effect of the parasympathomimetic drugs acetylcholine, pilocarpine, and physostigmine on the cerebral hemisphere gamma-aminobutyric acid (GABA) content was investigated before and after administration of atropine to adult male mice. Results indicate that these parasympathomimetic drugs significantly increased the GABA content. Atropine normalized the effect of the tested parasympathomimetic drugs, although it did not affect the cerebral GABA content. It is posited that the induced increase in the level of GABA, which is thought to be the main inhibitory transmitter in the cerebral cortex, is due to a compensatory and modulator mechanism released by the depolarizing action of cholinomimetic drugs. 18 references. (Author abstract modified)

002351 Sampson, Larry. University of Miami **Differential cardiovascular changes as a function of stimulation electrode site in rabbit hypothalamus. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 77-799 HC$15.00 MF$8.50 63 p.

Intracranial stimulation and selective autonomic blocking agents were used to examine the functional organization of the rabbit hypothalamus in terms of heartrate (HR) and blood pressure (BP) responses in chronically implanted Ss. Selective

autonomic blocking agents differentially influenced the various response patterns. While propranolol and atropine attenuated HR decrease to short pulse train stimulation, greater attenuation occurred under atropine. Phentolamine abolished BP and cardiodecelerative responses. Results suggested that the bradycardia response to high frequency, short pulse train stimulation is a baroreceptive reflex induced by arterial pressure increase. Atropine significantly reduced HR increase, but propranolol abolished it completely when using concomitant HR and BP increases elicited by long pulse train stimulation. For the HR increase/BP decrease pattern, propranolol almost totally abolished the tachycardia elicited by this stimulation, whereas atropine only partially attenuates it. In patterns of concomitant HR and BP decreases, both compounds attenuated HR decrease and propranolol virtually abolished it. Whereas the sympathetic innervation of the heart appears little involved in cardiovascular responses to high frequency, short pulse train hypothalamic stimulation plays a central role in elaborating various cardiovascular response patterns elicited by relatively low frequency, long pulse train stimulation. (Journal abstract modified)

002352 Sargent, T., III; Shulgin, A. T.; Kusubov, N. Donner Laboratory, University of California, Berkeley, CA 94720 **Quantitative measurement of demethylation of 14C-methoxyl labeled DMPEA and TMA-2 in rats.** Psychopharmacology Communications. 2(3):199-206, 1976.

It has been suggested that methylation and demethylation of compounds related to 6-hydroxydopamine may be involved in endogenous mental disorder such as schizophrenia. The synthesis of 3,4-dimethoxyphenethylamine (DMPEA) and 2,4,5-trimethoxyphenylisopropylamine (TMA-2) with each methoxyl group separately labeled with 14C is reported. The rate and percent demethylation of these two compounds, with five labeled positions, were determined in the rat. The results suggest that TMA-2 might be metabolized to a hydroquinone in vivo; a similar metabolic intermediate of the psychoactive compound DOM, the 4-methyl compound, is known to give rise in vitro to an indole. 10 references. (Author abstract)

002353 Sasa, Masashi. Department of Pharmacology, Faculty of Medicine, Kyoto University, Kyoto 606, Japan **Monoaminergic sensory regulation and the role of morphine.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):16P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March 1976, a study of the role of morphine in the monoaminergic sensory regulation of cats was reported. Recording of single spinal trigeminal nucleus (STN) neuron activities revealed that: 1) intravenous morphine and iontophoretically applied morphine blocked locus coeruleus (LC) induced inhibition of the orthodromic spike of relay neurons and type A neurons but did not affect dorsal raphe nucleus (DR) induced or sensory cortex (SC) induced inhibition; 2) systemic morphine did not affect the relay neuron or 80% of the type A neurons; 3) morphine inhibited the orthodromic spike generation of type B neurons; and 4) introphoresis of morphine did not affect orthodromic spike in all neurons. It is suggested that interneuron existing in STN, which is presumably a type A neuron, may produce an inhibition of orthodromic transmission in the relay neuron. Morphine releases the phasic inhibition form LC on A type neurons, thereby increasing the inhibitory effect on relay neurons. In addition, inhibition of transmission in long latency neurons, B type neurons, produced by morphine may also contribute to the analgesic effects of the narcotic. (Author abstract modified)

002354 Sastry, Bhagavatula Sree Rama; Sinclair, John Gordon. Division of Pharmacology and Toxicology, University of British Columbia, Vancouver, B.C., V6T 1W5, Canada **Serotonin involvement in the blockade of bulbospinal inhibition of the spinal monosynaptic reflex.** Brain Research (Amsterdam). 115(3):427-436, 1976.

Bulbospinal inhibition of the extensor quadriceps monosynaptic reflex (MSR) was antagonized by the serotonin precursor, 5-hydroxytryptophan (5-HTP), in unanesthetized, midcollicular, decerebrate cats. Fluoxetine hydrogen chloride (HCl), a specific serotonin neuronal uptake blocker, also blocked this inhibition as well as bulbospinal inhibition of the flexor posterior biceps semitendinosus MSR. The serotonin antagonist, cyproheptadine HCl, partially reversed the above blocking actions of 5-HTP and fluoxetine and enhanced bulbospinal inhibition when administered alone. Imipramine HCl was more potent in antagonizing bulbospinal inhibition of the dorsal root ventral root MSR when administered intraarterially to the spinal cord than when injected intraarterially to the brain stem or intravenously, indicating that the spinal cord is the site of impipramine's action. These results support the proposal that a 5-HT system antagonizes bulbospinal inhibition of the MSR. They also indicate that the 5-HT system is tonically active and exerts its blocking action in the spinal cord. 22 references. (Author abstract modified)

002355 Satoh, Hisashi; Satoh, Yoshihiko; Notsu, Yoshitada; Honda, Fumio. Research Laboratories, Fujisawa Pharmaceutical Co. Ltd., Osaka, Japan **Adenosine 3',5'-cyclic monophosphate as a possible mediator of rotational behaviour induced by dopaminergic receptor stimulation in rats lesioned unilaterally in the substantia nigra.** European Journal of Pharmacology (Amsterdam). 39(2):365-377, 1976.

A possible involvement of c-AMP in the rotational behavior induced by a stimulation of dopamine receptors in corpus striatum of rats was investigated. Rats were lesioned unilaterally in the substantia nigra with 6hydroxydopamine. Intraventricular injection of dopamine, norepinephrine and apomorphine induced rotational behavior towards the intact side as did dibutyryl c-AMP. Dopamine, norepinephrine and apomorphine could activate adenylate cylcase in homogenates of caudate nucleus. The activation by dopamine was blocked by haloperidol. I.p. injected apomorphine increased c-AMP content bilaterally in caudate nucleus and caused turning towards the intact side; theophylline potentiated and haloperidol blocked the effect. It is concluded that c-AMP acts as a second messenger in the central dopaminergic pathway in rats. 25 references. (Author abstract modified)

002356 Satomi, Ryuta, Asano, Yu; Saito, Yoshiro; Ohmiya, Tsukanobu; Kon, Yu; Okada, Fumihiko; Yamashita, Kaku; Suwa, Nozomu. Department of Neuropsychiatry, Hokkaido, University, Hokkaido, Japan **The biological dynamics of tricyclic antidepressants.** Psychiatria et Neurologia Japonica (Tokyo). 78(8):577, 1976.

In a paper presented at the 48th Hokkaido Psychoneurological Symposium held in December 1975 at Sapporo, Japan, the dynamics of the tricyclic antidepressant, amitriptyline, in the metabolism of rats were discussed. Rats were given 20mg/kg of amitriptyline and its absorption into the blood serum and organs was measured by gas chromatography. The metabolic product of amitriptyline, nortriptyline, was measured after one administration, after 1 week's administration, and after 2 weeks. Amitriptyline values in the cerebellum after one administration were from 4.5to 6.5mg/g, after 1 week were from 7.5to 9.5mg/g, and levels started falling off after 2 weeks. Nor-

triptyline disappeared within 24 hours after administration of amitriptyline.

002357 Sawada, H.; Hara, A. Department of Biochemistry, Gifu College of Pharmacy, Mitahora, Gifu 502, Japan **Novel metabolite of nitrazepam in the rabbit urine.** Experientia (Basel). 32(8):987-988, 1976.

Discovery of novel metabolites of nitrazepam in rabbit urine is described. Rabbit urine was collected for 48 hours after a single dose of 100mg/kg nitrazepam orally. The urine was extracted at pH9 with ethyl acetate, extract dried over anhydrous sodium sulfate and evaporated, and the residue was subjected to thin layer chromatography. The two novel metabolites were identified as 2-amino-3-hydroxy-5-nitrobenzophenone and 2'-benzoyl-4'-nitro-2-hydroxyacetanilide. The former was the major metabolite and was excreted mainly as the conjugated form. 7 references.

002358 Schwabe, U.; Miyake, M.; Ohga, Y.; Daly, J. W. Institut fur Pharmakologie, Medizinische Hochschule, Karl-Wiechert-Alles, D-3 Hannover 61 **4-(3-cyclopentyloxy-4-methoxyphenyl) 2-pyrrolidone (ZK-62 711): a potent inhibitor of cyclic AMP-phosphodiesterases in homogenates and tissue slices from rat brain.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 294(Supplement):R11, 1976.

In a paper presented at a pharmacology meeting in Hannover, Germany, on September 14-17, 1976, a new class of inhibitors of phosphodiesterases, represented by 4-(3-cyclopentyloxy-4-methoxyphenyl)-2-pyrrolidone, is discussed. This compound has potent central depressant activity and elicits significant elevations of cyclic nucleotide levels in rat brain slices. In rat cerebral homogenates, ZK 62 711 inhibited cyclic AMP-phosphodiesterases, while being less potent with respect to cyclic GMP phosphodiesterases. At low concentrations, ZK 62 711 was 100fold more potent than a structurally related phosphodiesterase inhibitor, Ro 20-1724, with respect to the calcium dependent cyclic AMP-phosphodiesterase. (Author abstract modified)

002359 Seeber, U.; Kuschinsky, K. Abteilung Biochemische Pharmakologie, Max-Planck-Institut fur Experimentelle Medizin, Hermann-Rein-Strasse 3, D-3400 Gottingen, Germany **Effects of penfluridol on dopamine-sensitive adenylate cyclase in corpus striatum and substantia nigra of rats.** Experientia (Basel). 32(12):1558-1559, 1976.

Penfluridol, a neuroleptic with diphenylbutyl piperidine structure, blocked the dopamine sensitive adenylate cyclase in homogenates of corpus striatum and substantia nigra of rats, probably by a competitive antagonism versus dopamine. These results indicate the occurrence of a dopamine stimulated adenylate cyclase in the substantia nigra of rats. The dopamine receptors in both brain regions seem to have a similar affinity for dopamine. The reason for the difference in the efficacy of dopamine might be either a difference in the density of dopamine receptors in both regions or a difference in the transmission from the receptors to the enzyme. The dopamine sensitive adenylate cyclase seems to be the in vitro system most appropriate for studying subcellular mechanisms of neuroleptics. 12 references.

002360 Sergeyev, P. V.; Vedernikova, N. N.; Mayskiy, A. I. Vtoroy Moskovskiy meditsinskiy institut im. N. I. Pirogova, Moscow, USSR **/Does the induction of microsomal liver enzymes cause tolerance of barbiturates?/** Yavlyaetsya li induktsiya mikrosomnykh fermentov pecheni prichinoy tolerantnosti k barbituratam? Farmakologiya i Toksikologiya (Moskva). 39(2):208-212, 1976.

Experiments were designed to compare the inductive capacity of different barbiturates and the development of tolerance to them. White female rats (experimental and control) were given injections of phenobarbital, sodium barbital, and sodium pentobarbital daily to analyze development of tolerance to productive barbiturates. The drugs produced activation of biosynthetic processes in liver cells after injection. The hypnotic effect disappeared 12 to 13 days after injections. Increase in the level of microsomal cytochromes correlated with their ability to stimulate synthesis of protein in a cell free system. The data exclude induction as a factor in the development of barbiturate tolerance. 13 references.

002361 Seyal, M.; Freeman, W. J. Department of Physiology/Anatomy, University of California, Berkeley, CA 94720 **Pharmacological study of evoked potentials in the olfactory bulb.** Physiologist. 19(3):362, 1976.

A study of the effects of synergists and antagonists of putative neurotransmitters on the rabbit olfactory bulb was presented. Drug effects were determined by measuring changes in the averaged evoked potential (AEP) induced by lateral olfactory tract stimulation. Muscarinic cholinomimetic agents caused an increase in frequency of the AEP, and nicotine caused an initial transient reduction in frequency. These effects suggest a selective increase in forward gain of the mitral cells. Atropine, scopolamine and dihydro-beta-erythroidine caused a reduction in frequency. Noradrenaline and the early effects of dexamphetamine caused a reduction in frequency, suggesting an increase in inhibitory bias. Reserpine, picrotoxin and phenoxybenzamine caused a reduction in frequency, interpreted as a reduction in forward gain of the granule population. GABA effects suggested multiple sites of action. (Author abstract)

002362 Shannon, Harlan E.; Holtzman, Stephen G. Department of Pharmacology, Emory University, Atlanta, GA 30322 **Blockade of the specific lethal effects of narcotic analgesics in the mouse.** European Journal of Pharmacology (Amsterdam). 39(2):295-303, 1976.

The capacity of the narcotic antagonists naloxone and nalorphine and the benzodiazepine derivatives diazepam and oxazepam to increase the LD50s of the narcotic analgesics morphine and methadone administered at convulsant doses was evaluated in the mouse. Naloxone and nalorphine produced a dose related increase in the LD50s of both morphine and methadone. Diazepam and oxazepma were also effective in increasing the LD50s of the narcotics; this effect was additive with that of naloxone. The anticonvulsant trimethadione did not elevate the LD50 of methadone, nor did it potentiate the effects of naloxone. Results suggest that the benzodiazepines may reduce the lethality of narcotic analgesics administered at high doses by a mechanism other than by an anticonvulsant effect alone. It is concluded that the capacity to increase the convulsant LD50 of the narcotic analgesics is a general property of the narcotic antagonists. 18 references. (Author abstract modified)

002363 Shelenkova, S. A. Permskiy farmatsevticheskiy institut, Perm, USSR **/Effect of combined introduction of 2-methyl 3 (o-chlorphenyl) quinazolone-4 and phenobarbital with hydrocortisone on blood corticosteroid content and ATP-ase activity in the rat./** Vliyaniye kombinirovannogo vvedeniya fenobarbitala i 2-metil-3-(o-khlorfenil)-khinazolona-4 s gidrokortizonom na dinamiky soderzhaniya kortikosteroidov v krovi i atf-aznuyu aktivnost' golovnogo mozga krys. Farmakologiya i Toksikologiya (Moskva). 39(5):529-531, 1976.

The blood corticosteroid level was investigated in 60 white rats given combined injections of hydrocortisone with 2-methyl-3-(o-chlorphenyl)-quinazolone-4 and phenobarbital, using a fluoroscopic method. The effect of these combinations on ATP-ase activity was studied as well, with the level of inorganic phosphorus as the index. The combined injection produced a reverse dynamic connection between the level of corticosteroids in the blood and the level of soporific activity. The link between the soporific effect and the degree of depression of ATP-ase activity in the homogenized brain tissue was very clear in tests with phenobarbital, not so clear with 2-methyl-3(o-chlorphenyl)-guinazolone-4. 18 references.

002364 Sherman, A. D.; Gal, E. M. Neurochemical Research Laboratories, Dept. of Psychiatry, University of Iowa College of Medicine, 500 Newton Road, Iowa City, IA 52242 **Mass-spectrographic evidence of the conversion of p-chloroamphetamine to 3,4-dimethoxyamphetamine.** Psychopharmacology Communications. 2(5&6):421-427, 1976.

Intraventricularly injected p-chloroamphetamine (p-CA) was actively metabolized to 3, 4-dimethoxyamphetamine (3, 4-DMA) in the rat brain. Time course experiments with intraperitoneally injected p-CA confirmed that the presence of cerebral 3, 4-DMA was not due to its "one-pass" entry from the peripheral organs. The identity of 3, 4-DMA from brain tissue and urine was established by comparison to authentic 3, 4-DMA. The synthetic and biological samples were isographic in all analytical systems. 3, 4-DMA from biological samples was verified by mass spectography. 5 references. (Author abstract modified)

002365 Shibuya, Takeshi; Sato, Katsuhiko; Matsuda, Hiromi; Nishimoi, Tsukao; Hayashi, Masaaki; Nomura, Kaoru; Chen, Po Chung. Department of Pharmacology, Tokyo Medical College, Tokyo 160, Japan **Effects of benzodiazepines on brain monoamines.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):102P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March 1976, a study of the effects of four benzodiazepines (diazepam, triazolam, chlordiazepoxide, and prazepam) on rat brain monoamine (norepinephrine, dopamine, and serotonin) concentrations and monoamine metabolism was reported. Administration of the benzodiazepines alone produced no changes in the monoamine levels in any area of the brain. The drugs did inhibit the decrease in catecholamine concentration produced by blockade of tyrosine beta-hydroxylase. It is concluded that the CNS effects of benzodiazepines are associated with their effects on monoamine metabolism. (Author abstract modified)

002366 Shimada, Akira; Iizuka, Hiromi; Yanagita, Tomoji; Shibata, Katsutoshi. Department of Pharmacology, Central Institute for Experimental Animals, Kawasaki 211, Japan **Cortical evoked potentials as a parameter of the development of tissue tolerance and physical dependence.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):42P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study which used cortical evoked potentials in an examination of the development of tissue tolerance and physical dependence in rats was reported. Male rats were treated with barbital or with morphine twice daily for 4 weeks. When rats were given the first administration of barbital, their coordinative motion was markedly impaired. Motor coordination gradually recovered even after a dose increase from the 3rd week and on the 28th day of the treatment, motor coordination was only slightly impaired. Serum concentration slightly decreased in the last 2 weeks. A single dose of barbital or morphine prolonged the latent time of the evoked potential in the control rats, but not in the treated animals. The latent time in the treated and withdrawn rats became shorter than that of the untreated rats, especially in the morphine withdrawn rats. It is suggested that the cortical evoked potentials can be a useful parameter for the observation of the development of tissue tolerance to and physical dependence on barbital or morphine. (Author abstract modified)

002367 Shinohara, Mami; Sakurada, Osamu; Jehle, Jane; Sokoloff, Louis. National Institute of Mental Health, Bethesda, MD 20857 **Effects of D-lysergic acid diethylamide on local cerebral glucose utilization in the rat. (Unpublished paper).** Laboratory of Cerebral Metabolism, NIMH, 1976.

An autoradiographic radiolabeled dioxyglucose method which provides a means of measuring the rates of glucose consumption simultaneously in all the functional components and structural components of the brain visible macroscopically in the autoradiographs was used in an effort to define the areas of the rat brain altered by lysergic acid diethylamide (LSD). LSD produces dose dependent reductions in glucose utilization in selected cerebral structures. With increasing doses more and more structures are affected and the effects are of greater magnitude. A pattern of distribution of effects among the various cerebral structures that might explain the drug's psychotogenic effects has not been discernible. (Author abstract modified)

002368 Shumilina, A. I.; Burza, Zh. B. Lab. of Gen. Physiol. of the CNS, Inst. of Normal and Pathological Physiology, Academy of Med. Sci. USSR, Moscow, USSR **Multiplication of the late slow component of the evoked potential to light during chlorpromazine administration.** Neuroscience and Behavioral Physiology. 7(1):20-23, 1976.

In experiments on unanesthetized rabbits with electrodes permanently implanted in various brain formations the effect of chlorpromazine on multiplication of late slow component of evoked potential produced by flashes of light was studied. Some flashes were applied simultaneously with electric shock to the hind limb. Chlorpromazine was found to reduce multiplication of the slow component to flashes applied without electric shocks and to facilitate reduplication of this component in response flashes coupled with electric shock. A role of adrenergic structures in the formation of the defensive action acceptor is postulated. 7 references. (Journal abstract modified)

002369 Siggins, G. R.; Hoffer, B. J.; Bloom, F. E.; Ungerstedt, U. Laboratory of Neuropharmacology, Division of Special Mental Health Research, NIMH, St. Elizabeths Hospital, Washington, DC 20032 **Cytochemical and electrophysiological studies of dopamine in the caudate nucleus.** In: Yahr, Melvin D., The basal ganglia. Vol. 55. New York, Raven Press, 1976. 474 p. (p. 227-248).

In a paper presented at the 55th meeting of the Association for Research in Nervous and Mental Disease, cytochemical and electrophysiological studies of dopamine in the rat caudate nucleus were reviewed to demonstrate the effects of iontophoretically applied dopamine, apomorphine, cyclic AMP, and drugs (such as prostaglandin E) on cyclic AMP metabolism, as well as the effects of noncyclic adenine derivatives. Results using 6-hydroxydopamine injections show involvement of cyclic AMP in inhibitory responses of caudate neurons to both locally applied dopamine and adenosine and suggest that

the nigrostriatal dopamine pathway inhibits cellular discharge by intermediation of a cyclic AMP second messenger system, which can also be activated via adenosine. Findings conclusively suggest cyclic AMP as the functional mediator for the profuse innervation of caudate by nigral dopamine fibers, and have implications for such clinical problems as Parkinson's disease, in which there is evidence for reduced dopamine input to caudate neurons. 75 references.

002370 Slotkin, Theodore A.; Lau, Christopher; Bartolome, Maria; Seidler, Frederic J. Department of Physiology and Pharmacology, Duke University Medical Center, Durham, NC 27710 **Catecholamine synthesis, storage and release in adrenal medulla and whole brain during acute and chronic methadone administration.** Biochemical Pharmacology (Oxford). 25(22):2523-2527, 1976.

Catecholamine synthesis, storage, and release in the adrenal medulla and whole brain during acute and chronic methadone administration were examined. Methadone was administered daily to rats and the adrenals were analyzed for catecholamines, tyrosine hydroxylase activity and dopamine-beta-hydroxylase activity. Methadone increased the rate of formation of new adrenal storage vesicles and inhibited catecholamine uptake into the vesicles, an effect which was also observed with methadone in vitro. Similarly, methadone in vitro inhibited amine uptake into crude whole brain synaptosomes, but the effect was not observed after acute or chronic administration in vivo. It is concluded that methadone, like morphine, stimulates the sypatho-adrenal axis, but that unlike morphine, methadone exerts a direct effect on adrenal storage vesicles. 22 references. (Author abstract modified)

002371 Sloviter, Henry A. University of Pennsylvania, Philadelphia, PA 19174 **Effects of psychoactive agents on the brain.** Final Report, NIMH Grant MH-20946, September, 1976. 7 p.

Isolated perfused rat brains administered the narcotic analgesics morphine and methadone were investigated to study the effects of these drugs on the metabolic, histochemical and electrical behavior. Dimethylsulfoxide (DMSO), an agent facilitating transport of drugs and neurotransmitters across the blood-brain barrier, caused an increase in the glycolytic rate of isolated brain, a slight decrease in the energy reserves and a shift to a reduced state in the cerebral tissue. Perfusion of isolated brain with morphine increased glucose utilization and lactate production, decreased levels in cerebral tissue of creatine phosphate and ATP and changes in glycolytic intermediates which suggests that morphine interferes with cellular oxidative activity. Perfusion with methadone caused increased glucose utilization, but no increase in lactate production and no changes in the levels of creatine phosphate or ATP. In histological section, after methadone infusion, norepinephrine in the supraoptic nucleus decreased and turnover of dopamine in the caudate-putamen probably increased. Morphine and methadone decreased the level of vasopressin in the supraoptic nucleus of the perfused rat brain. Methadone caused sharp waves, spikes and seizure activity in the brain of the intact rat and in the perfused brain.

002372 Spano, P. F.; Kumakura, K.; Trabucchi, M. Department of Pharmacology and Pharmacognosy, University of Milan, Milan, Italy **Dopamine-sensitive adenylate cyclase in the retina: a point of action for D-LSD.** Advances in Biochemical Psychopharmacology. 15:357-365, 1976.

Studies of the interaction of lysergic acid diethylamide (LSD) with central dopamine (DA) receptors and particularly with limbic and retinal DA sensitive adenylate cyclases are reported. In vitro experiments have revealed that LSD increases the formation of cyclic adenosine monophosphate (cAMP) in rat striatum, nucleus accumbens, tuberculum olfactorium, and limbic cortex but not in the cerebellum where no DA terminals or DA sensitive adenylate cyclase have been described. It was also found that 2-bromo-LSD, which is devoid of hallucinogenic properties, has no effect on the DA sensitive adenylate cyclase in rat striatum. Pretreatment of the animals with LSD prior to testing inhibited the stimulation of cAMP formation by DA. The data indicate a common site of action for DA and LSD on the DA sensitive adenylate cyclase and suggest a central interaction of LSD with DA. The possible interaction of LSD with DA sensitive adenylate cyclase in the retina was examined in the rat, rabbit, cat, and calf. LSD exerted a significant stimulatory effect on the adenylate cyclase activity of retina homogenates in all species studied. Haloperidol inhibited the stimulation of rat retina adenylate cyclase by both DA and LSD. An enhancement of the effects of DA and LSD was noted in light deprived rats, suggesting a possible light deprivation induced supersensitivity at the level of the postsynaptic DA receptor. It is concluded that LSD is a DA agonist in the retina of all species tested, and it is suggested that this action may be related to the ability of LSD to produce visual hallucinations. 21 references.

002373 Speckenbach, Wolfgang; Kehr, Wolfgang. Dept. fur Neuropharmakologie, Schering AG, Mullerstrasse 170-178, D-1000 Berlin 65, Germany **Effect of (.)amphetamine on monoamine synthesis and metabolism after axotomy in rat forebrain.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 296(1):25-30, 1976.

To study the effect of (.)amphetamine on catecholamine synthesis and metabolism in the terminal system, changes in impulse flow were eliminated by cutting the ascending monoaminergic axons in the forebrain of male rats. Axotomy resulted in a 3 fold increase in Dopa formation in the lesioned forebrain during 30 min after inhibition of the aromatic amino acid decarboxylase with 3-hydroxybenzylhydrazine HCl. (.)-amphetamine sulfate, 10 mg/kg i.p. antagonized the hemisection induced increase in Dopa formation and reduced the formation of 5-hydroxytryptophan. Pretreatment with haloperidol failed to counteract the effect of (+)amphetamine. In the intact forebrain the stimulation of Dopa accumulation was more than additive after combined treatment with haloperidol and (+)amphetamine. Hemitransection retarded the disappearance of dopamine and noradrenaline after administration of alpha-methyl-p-tyrosine methylester HCl. (+)amphetamine, accelerated the utilization of dopamine on the lesioned side. Hemitransection reduced the formation of 3-methoxytyramine during 1 h after pargyline. After (.)amphetamine 3-methoxytyramine formation in the intact forebrain was 3 times higher than in the lesioned forebrain. The action of (.)amphetamine on dopamine synthesis and release appears to be dependent on the firing rate in dopamine neurons. 33 references. (Author abstract)

002374 Stang, D.; Martin, J. B. Department of Psychiatry, Montreal General Hospital and McGill University, Montreal, Quebec, Canada **Effect of hypothalamic hormones on the concentration of adenosine 3',5'-monophosphate in incubated rat pineal glands.** Life Sciences (Oxford). 19(6):911-918, 1976.

The effect of hypothalamic hormones on the adenylate-cyclase cyclic adenosine 3',5'-monophosphate (cyclic AMP) generating system in rat pineal glands was investigated. Aliquots of prepared pineal glands were assayed for cyclic

AMP by the protein binding assay method, and protein was determined by the Lowry method using bovine serum albumin as a standard. Norepinephrine stimulated accumulation of cyclic AMP was inhibited by thyrotropin releasing hormone (TRH), but not by DDD-TRH, an inactive analog. Luteinizing hormone releasing hormone (LRH) was less effective than TRH, and somatotropin release inhibiting factor had effects only at high concentration. Findings demonstrate that TRH, and to a lesser extent LRH, are potent inhibitors of norepinephrine stimulated cyclic AMP accumulation in the pineal gland. The formation of melatonin in the pineal gland as increased by norepinephrine, which activates adenylate cyclase to cause an increase in synthesis of cyclic AMP, suggests that cyclic AMP may be the physiological regulator of melatonin biosynthesis. Results thus provide biochemical evidence of an interaction between hypothalamic hormones and noradrenergic function, providing a hypothesis concerning a physiological role of these peptides in the pineal gland. 25 references. (Author abstract modified)

002375 Steinberg, Michael S.; Doctor, B. P. Dept. of Hematology, Div. of Medicine, Walter Reed Army Institute of Research, Washington, DC 20012 **Studies on the effect of 5,5′-diphenylhydantoin on in vitro protein synthesis in rat brain.** Journal of Pharmacology and Experimental Therapeutics. 198(3):648-654, 1976.

The effect of 5,5′-diphenylhydantoin (DPH) on in vitro protein synthesis was studied by investigating the possible role of DPH on poly-Uracil directed polyphenylalanine synthesis and natural mRNA directed amino acid incorporation into polypeptides. There was no demonstrable effect on DPH on either of these reactions. In addition, DPH did not alter the rate of aminoacylation of purified rat liver tRNAs. The in vivo daily administration of DPH to rats did not appear to affect the in vitro poly-Uracil directed polyphenylalanine synthesis (chain elongation aspects of protein synthesis) in adult rat brain. DPH did not inhibit DNA dependent RNA synthesis as catalyzed by RNA polymerase. The results do not support the hypothesis that DPH plays a role in protein synthesis in adult brain cells. 26 references. (Author abstract modified)

002376 Stillwell, W. G.; Myran, C. S.; Stewart, J. T. Institute for Lipid Research, Baylor College of Medicine, Houston, TX 77030 **Meperidine metabolites: identification of N-hydroxynormeperidine and a hydroxymethoxy derivative of meperidine in biological fluids.** Research Communications in Chemical Pathology and Pharmacology. 14(4):605-619, 1976.

Combined gas chromatographic and mass spectrometric procedures were used to characterize the N-oxgenated metabolites of meperidine (N-methyl-4-phenyl-4-carbethoxypiperidine) in human, rat, and guinea pig urine, and thin layer chromatography was used to separate N-hydroxynormeperidine from the expected metabolites normeperidine and meperidine N-oxide. In rat urine the p-hydroxyphenyl metabolite of meperidine was present in appreciable amounts. Also present in small quantity was a new phenolic metabolite of meperidine containing both hydroxyl and O-methoxyl substituents in the phenyl ring of the parent drug. The latter two metabolites were excreted as conjugates in the rat. The data suggest that N-hydroxynormeperidine is an important metabolic pathway in the human. 20 references. (Author abstract modified)

002377 Stone, Eric A. Millhauser Laboratories of the Department of Psychiatry, New York University Medical Center, New York, NY 10016 **Central noradrenergic activity and the formation of glycol sulfate metabolites of brain norepinephrine.** Life Sciences (Oxford). 19(10):1491-1498, 1976.

Intraventricular injection of S35-labeled sodium sulfate was used to detect drug induced changes in the in vivo formation of the two major metabolites of rat brain norepinephrine (NE) -- the sulfate conjugates of 3-methoxy-4-hydroxyphenylglycol (MOPEG-SO4) and 3,4-dihydroxyphenylglycol (DOPEG-SO4). Assays involved the hypothalamus only. Rats pretreated with clonidine showed a reduced formation of both MOPEG-labeled SO4 and DOPEG-labeled SO4 after intraventricular labeled sodium sulfate as well as a reduced synthesis of 3H-NE from intraventricular 3H-tyrosine. Phenoxybenzamine (POB) produced increases in the synthesis of both 35S-labeled conjugates and 3H-NE. Neither drug altered the loss of exogenous 3H-MOPEG-SO4 but clonidine increased both the accumulation of labeled sulfate and the sulfation of exogenous MOPEG in pheniprazine treated rats. These results show that the rates of formation of the labeled glycol sulfates are sensitive indicators of changes in brain NE turnover but can also be influenced by factors involved in sulfation that are unrelated to NE turnover. Blockade of NE synthesis with alpha methyltyrosine did not affect resting or POB elevated levels of the labeled conjugates until stores of NE were reduced by 40% . The latter findings suggest that central noradrenergic neurons can release and metabolize NE at a normal rate despite synthesis blockade so long as adequate stores of NE are available. 29 references. (Author abstract)

002378 Sugimoto, Jiro; Ikeda, Yoshihiro; Shimamoto, Juno; Morita, Masao. Department of Pharmacology, Kansai Medical School, Moriguchi 570, Japan **Comparative studies on the actions of chlorpromazine and diazepam in isolated rat heart.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):133P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March 1976, a study of the actions of chlorpromazine and diazepam on the spontaneously beating right atrium, left atrium and papillary muscle of the rat were reported. Arrhythmic contractions of right atrium induced by electrical square wave stimulation were prevented by diazepam while little prevention was seen with chlorpromazine. Contractile tensions of the left atrium and papillary muscle driven by suprathreshold electrical stimulation were depressed by a diazepam concentration higher than 0.02mg/ml or by a chlorpromazine concentration higher than 2 micrograms/ml. Diazepam dose dependently increased the left atrial and papillary muscle tensions. Chlorpromazine had no significant effect on the left atrial muscle tension but dose dependently suppressed papillary muscle tension. The refractory periods of left atrium and papillary muscles were increased by diazepam and chlorpromazine. It is suggested that not only the psychopharmacologie action of diazepam but also the cardiac action plays a role when the drug is used as an adjunct in the management of patients with arrhythmias. (Author abstract modified)

002379 Sze, Paul Y. Department of Biobehavioral Sciences, University of Connecticut, Storrs, CT 06268 **Glucocorticoid regulation of the serotonergic system of the brain.** Advances in Biochemical Psychopharmacology. 15:251-265, 1976.

Recent studies indicating the involvement of glucocorticoids in the biosynthesis of brain serotonin (5-hydroxytryptamine, 5-HT) are summarized with emphasis on the regulation by these hormones of tryptophan hydroxylase activity and tryptophan levels. Bilateral adrenalectomy in 9-day-old rats prevented the developmental increase of tryptophan hydroxylase activity in

whole brain. Replacement injections of corticosterone restored the enzyme activity to above normal levels. Corticosterone also induced tryptophan hydroxylase activity in intact rats. The inducibility of tryptophan hydroxylase by glucocorticoids during early development of the rat correlated with the developmental changes in brain corticosterone levels. Increases in brain tryptophan hydroxylase induced by reserpine injection of chronic alcohol ingestion did not occur in adrenalectomized mice but this effect on the drugs was restored after steroid replacement. A single injection of hydrocortisone acetate (HCA) increased tryptophan levels in mouse whole brain. This increase was localized in the synaptosomal fraction. HCA decreased the steady state levels of brain 5-HT but increased the 5-HT turnover rate. In vitro, HCA increased the uptake of radiolabeled tryptophan by isolated brain synaptosomes. It is posited that glucocorticoids regulate 5-HT synthesis via an increased uptake of tryptophan by nerve terminals and by an induction of tryptophan hydroxylase by mechanisms yet to be identified. 49 references.

002380 Tabakoff, Boris; Moses, Frances. Department of Physiology, University of Illinois Medical Center, Chicago, IL 60612 **Differential effects of tranylcypromine and pargyline on indoleamines in brain.** Biochemical Pharmacology (Oxford). 25(23):2555-2560, 1976.

The effects of tranylcypromine and pargyline on general activity and body temperature and on levels of tryptophan and the synthesis of serotonin in the brain were studied in male C57B1/6 mice. Activity was measured in a test cage over 3 min periods, and body temperature was determined rectally. Brain levels of tryptophan and serotonin were assayed after separation of these compounds by column chromatography. Body temperature was found to be unchanged after tranylcypromine, and lowered after pargyline. Activity increased after tranylcypromine treatment and decreased after pargyline treatment. At doses which inhibited monoamine oxidase, tranylcypromine significantly raised brain tryptophan levels, while pargyline had no effect. The rise in brain tryptophan levels was accompanied by increases in free tryptophan levels in plasma. The increase in brain tryptophan with tranylcypromine did not lead to significant increases in accumulation of serotonin, as compared with pargyline treated animals. After tranylcypromine treatment, there appears to be an accumulation of indoleamines other than serotonin, accounting for the above results. 33 references.

002381 Takahashi, Ryo; Tachiki, Ken H.; Nishiwaki, Kenzaburo; Nakamura, Eitoku; Tateishi, Toshiaki; Nagayama, Haruo. Department of Neuropsychiatry, Nagasaki University School of Medicine, Nagasaki, Japan **Biochemical basis of an animal model of depressive illness -- a preliminary report.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 30(2):207-218, 1976.

The results of behavioral tests and biochemical analyses conducted on a rat which was sacrificed during a behavioral state of motionlessness (animal model of depression) induced by conditioned reflex techniques. To achieve this state, a sound stimulus is paired with an injection of tetrabenazine (TBZ) and conditioning is considered established when the animal develops a state of motionless on presentation of the sound stimulus alone. The state of motionless was found to be due to an excess functional activity of serotonin (5-hydroxytryptamine, 5HT) and it is suggested that an excess of functional activity of 5HT may be responsible for human depressive illness. This conclusion is in conflict with currently popular theories of depression. Animal and clinical data in the literature which are consistent with this conclusion are presented and discussed. The results are also discussed in terms of the proposed mechanism of action of TBZ. 61 references. (Author abstract)

002382 Tarve, U. S.; Paesalu, E. I.; Tyakhepyl'd, L. Ya. Tartuskiy universitet Estonskoy SSR, Tartu, USSR /**Comparative study of the effect of certain psychotropic drugs on brain Na+, K+-ATPase activity in vitro.**/ Sravnitel'noye izucheniye vliyaniya nekotorykh psikhotropnykh veshchestv na atktivnost' Na+, K+ATF-azy mozga in vitro. Ukrainskiy Biokhimichniy Zhurnal (Kiev). 48(3):326-331, 1976.

The effects of certain neuroleptics (levomepromazine, chlorpromazine, perphenazine and haloperidol), antidepressants (imipramine and iproniazid) and psychostimulants (amphetamine), plus the effects of benactyzine and procaine were studied in bovine brains in vitro. These drugs evoked different degrees of enzyme inhibition. Sensitivity of the brain sodium ATPase and potassium ATPase to the drugs decreased in the following order: levomepromazine, chlorpromazine, perphenazine, haloperidol, imipramine, iproniazid, benactyzine, procaine and amphetamine. Competition for the enzyme was observed between sodium and some of the drugs and between potassium and other drugs. Inhibition of brain sodium ATPase and potassium ATPase by psychotropic drugs may be part of the biochemical mechanism of their sedative/tranquilizing activity. 18 references. (Journal abstract modified)

002383 Thomsen, Klaus; Olesen, Ole Vendelin; Jensen, Jorgen; Schou, Mogens. Psychopharmacology Research Unit, Aarhus University, Risskov, Denmark **Mechanism of gradually developing lithium intoxication in rats.** In: Essman, W., Current developments in psychopharmacology. New York, Spectrum, 1976. 393 p. v. 3. (p. 155-177).

Studies of the involvement of sodium ion levels in the development and course of lithium intoxication in rats are reviewed. It has been found that lithium administration lowers the renal response to sodium retaining hormones, resulting in a rise of the minimum sodium requirement. If the sodium requirement should exceed sodium intake, the organism loses sodium and sodium deficiency develops. Renal clearance of lithium is lowered, resulting in an increase of serum lithium concentration and consequent aggravation of the sodium deficiency. This circle progresses until the death of the animal. Administration of sodium chloride abolishes the sodium deficiency and breaks the circle. The rat model seems applicable to man as far as the initiation of a gradually developing lithium intoxication is concerned. Once lithium intoxication has developed, humans differ from rats in showing less striking response to sodium chloride administration and additional therapeutic measures are indicated. 40 references. (Author abstract modified)

002384 Tokunaga, Yukiko; Muraki, Takamura; Yasuyama, Masako; Kondo, Yuko; Hosoya, Eikichi. Department of Pharmacology, Keio University School of Medicine, Tokyo 160, Japan **Effect of morphine on the hypothalamo-pituitary-gonadal axis of morphine-tolerant rats.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):121P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March 1976, a study of the effect of morphine on the hypothalamopituitary/gonadal axis of morphine tolerant rats was reported. Serum concentration of testosterone and gonadotropins and hypothalamic content of luteinizing hormone releasing factor (LRF) of morphin-

tolerant rats were determined by radioimmunoassay. Serum concentration of testosterone and luteinizing hormone (LH) of morphine tolerant rats was lower than that of saline control rats during 2 to 12 hr after the last dose of morphine and returned to control levels between 24 and 72 hr. Hypothalamic levels of LRF in morphine tolerant rats was within the range of saline controls. Serum concentration of follicle stimulating hormone (FSH) was variable and did not change in parallel to that of testosterone or LH. It is suggested that the low sperm content of epididymis and the reduced weight of male accessory reproductive organs in morphine tolerant rats may be the result of repeated transient depression of serum concentration of testosterone caused by morphine. (Author abstract modified)

002385 Traficante, L. J.; Friedman, E.; Oleshansky, M. A.; Gershon, S. Department of Psychiatry, New York University School of Medicine, 550 First Avenue, New York, NY 10016 **Dopamine-sensitive adenylate cyclase and cAMP phosphodiesterase in substantia nigra and corpus striatum of rat brain.** Life Sciences (Oxford). 19(7):1061-1066, 1976.

A dopamine sensitive adenylate cyclase and cyclic adenosine monophosphate (cAMP) phosphodiesterase in substantia nigra and corpus striatum of the rat brain were studied. Low concentrations of dopamine markedly increased the accumulation of cyclic AMP while l-norepinephrine and isoproterenol had little effect at concentrations up to 100uM. Trifluoperazine was a potent inhibitor of the substantia nigral adenylate cyclase while the adrenergic receptor blocking agents propranolol and phentolamine were ineffective. Basal activity of striatal adenylate cyclase and cAMP phosphodiesterase was approximately three fold higher than that found in substantia nigra. 15 references. (Author abstract)

002386 Tsuchiya, Toshiro; Fukushima, Hideaki; Kitagawa, Sumio. Institute for Biological Science, Pharmaceuticals Division, Sumitomo Chemical Co., Ltd., Takarazuka, Hyogo 665, Japan **Effects of benzodiazepines on evoked potentials induced in the limbic system and hypothalamus in the cat brain.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):94P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study of the effects of benzodiazepines on evoked potentials in the limbic system and hypothalamus of the cat brain was reported. The benzodiazepines affected various neuronal connections in the systems studied, especially the amygdala (AMYG), ventromedial hypothalamus (VMH), and central gray matter (SCG). Hippocampal (HIPP) evoked potentials were attenuated, but those of the AMYG/VMH, VMH/AMYG, and septum (SP) VMH were facilitated. Both benzodiazepines and pentobarbital affected three afferent hippocampal neuronal connections, areas of the reticulo/hypothalamic system regulating hippocampal activity. However, only the benzodiazepines affected the neuronal influence of the amygdala and septum on the hypothalamus. The effects of several new 1,4-benzodiazepine derivatives were also studied. These compounds were found to have a more narrow action than diazepam, with specific effects on AMYG/HIPP and AMYG/VMH evoked potentials in the limbic/hypothalamic circuit and on the SGC/HIPP evoked potential which is involved in the regulation of the hippocampal theta wave. (Author abstract modified)

002387 Tsuchiya, Toshiro; Kitagawa, Sumio. Pharmaceuticals Division, Sumitomo Chemical Co., Ltd., Takarazuka Hyogo 665, Japan **Effects of benzodiazepines and pentobarbital on the evoked potentials in the cat brain.** Japanese Journal of Pharmacology (Kyoto). 26(4):411-418, 1976.

The sites of action of two benzodiazepines, diazepam and 1D-540 7-chlore-5-(ortho-fluorophenyl)-1-methyl-1,3-dihydro-2H-1,4-benzodiaze ine-2-one) on the CNS were examined and compared with those of pentobarbital using evoked potentials recorded on the limbic system and hypothalamus in the cat brain. The benzodiazepines attenuated amygdala/hippocampal (AMYG/HIPP), ventromedial hypothalamus VMH/HIPP and central gray matter SGC/HIPP evoked potentials and facilitated AMYG/VMH, VMH/AMYG and septum SP/VMH evoked potentials. Pentobarbital selectively attenuated the SGC/HIPP, VMH/HIPP and AMYG/HIPP evoked potentials and facilitated the VMH/AMYG and SP/HIPP evoked potentials. The benzodiazephines and pentobarbital both affected three afferent hippocampal neuronal connections, areas of the reticulohypothalamic systems regulating hippocampal activity, while only the benzodiazepines affected the neuronal influence of the amygdala and septum on the hypothalamus. 19 references. (Author abstract modified)

002388 Tyce, Gertrude M.; Sharpless, Nansie S.; Owen, Charles A., Jr. Department of Biochemistry, Mayo Clinic and Mayo Foundation, Rochester, MN 55901 **Metabolism of 3-O-methyldopa by the isolated perfused rat liver.** Biochemical Pharmacology (Oxford). 25(23):2635-2641, 1976.

The disposition and metabolism of 3-O-methyldopa, a metabolite of L-dopa, was studied in the isolated perfused rat liver system. The 3-O-methyldopa caused an increase in the flow of bile. C14-labeled 3-O-methyldopa was injected, and its rate of disappearance from whole blood, plasma, red blood cells, and liver, as well as its rate of appearance in the bile, were measured over a 5 hour period. During perfusion, most of the 3-O-methyldopa remained unmetabolized, with a variety of metabolites being present in small amounts. Demethylation of 3-O-methyldopa to dopa occurred in the erythrocytes. 28 references.

002389 Uchida, Yoko; Nomoto, Teruko. Department of Pharmacology, Tokyo Women's Medical College, Tokyo 162, Japan **Influence of adrenal enucleation on thermal response to chlorpromazine in rats.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):148P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March 1976, a study of the influence of adrenal enucleation on thermal response to chlorpromazine (CPZ) in rats was reported. On the 3rd day after enucleation, adrenal weight was reduced to 75% that of controls and was about 85% of the initial value when the experiments were carried out. Noradrenaline (NA) level in the hypothalamus was unaffected by enucleation. For 3 to 7 da after enucleation, there was a decline in NA content of the cerebral cortex, heart, and submaxillary gland, but no alteration was found a month after the surgery. In sham operated rats, the rectal temperature decreased 1 hr after the injection of CPZ and recovered to the baseline level within 6 to 7 hr. The CPZ related hypothermia was not observed in all adrenal enucleated cats. CPZ injection also caused hyperglycemia in sham operated rats but not in adrenal enucleated rats. It is suggested that the decrease in rectal temperature induced by CPZ is partially mediated by catecholamines released from adrenal medula. The hyperglycemia may also be the result of the release of catecholamines. (Author abstract modified)

002390 Ueno, Akira; Nonaka, Kazuko. Department of Pharmacology and Experimental Therapeutics, Nagasaki University

School of Medicine, Nagasaki 852, Japan **Effects of some drugs on the coronary circulation in unanesthetized and unrestrained dogs.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):136P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March 1976, a study of the effects of psychoactive drugs on the coronary blood flow in unanesthetized and unrestrained dogs was reported. When morphine, chlorpromazine and droperidol were given subcutaneously and pentazocine, imipramine and dimorpholamine were given intravenously (iv), there was almost no change in the coronary blood flow and coronary resistance. A moderate decrease in the coronary blood flow and an increase in coronary resistance were exhibited after a large dose of nikethamide given iv and a regular dose of clonidine given iv. Eserine given iv caused a rise of the blood pressure with increasing coronary resistance. (Author abstract modified)

002391 Ukai, Makoto; Nabeshima, Toshitaka; Kameyama, Tsutomu. Department of Chemical Pharmacology, Faculty of Pharmaceutical Sciences, Meijo University, Nagoya 468, Japan **Effects of various drugs on morphine-induced Straub response in mice (II): the relationship between GABA derivatives and tail response.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):118P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March 1976, a study of the effects of difenamizole (DFZ); (1,3-diphenyl-5-(2-dimethylaminopropionamide)-pyrazole) on brain 5-hydroxytryptamine (serotonin, 5-HT) content in mice was reported. The relationship between gamma-aminobutyric acid (GABA) derivatives and the morphine induced Straub tail response (SR) was also investigated. Brain 5-HT content of the cerebellum and the diencephalon significantly increased in DFZ treated animals compared with vehicle treated animals. GABA inhibited the morphine induced SR. In animals given DFZ concomitantly with GABA, the SR was decreased significantly at 30 min after morphine, as compared with animals given DFZ alone. The results suggest that the SR is inhibited with the increase fo 5-HT in the cerebellum and the diencephalon. The possibility that GABA may prevent the SR by means of an inhibitory action on the central nervous system in mice was pointed out. (Author abstract modified)

002392 Uzan, A.; Gueremy, C.; Le Fur, G. Recherche et Pharmacie, S.A., Produits Chimiques Ugine-Kuhlmann, 35, quai du Moulin de Cage, F-92231 Gennevilliers, France **/Absorption, distribution and elimination of 10-(3-quinuclidinylmethyl) phenothiazine (LM 209), a new antiallergenic.** Absorption, distribution et excretion de la (quinuclidinyl-3 methyl)-10 phenothiazine (LM 209), un nouvel anti-allergique. Xenobiotica (London). 6(10):633-648, 1976.

The absorption, distribution, and elimination of 10-(3-quinuclidinylmethyl)-phenothiazine (LM 209) were studied in rats and dogs after oral or intravenous administration of the 35S labeled molecule. Determination of radioactivity confirmed absorption and showed that the blood levels increase in proportion to the dose but remain very low compared with tissue concentrations, which were highest in the liver and lung and persisted at a high level for more than 6 hours. A high level of radioactivity in feces resulted mainly from biliary excretion, which was accompanied by much enterohepatic circulation. The prolonged retention of LM 209, due to binding to blood and tissue proteins and to enterohepatic circulation, did not lead to noticeable accumulation of the drug after repeated doses. The difference in the intracellular distribution of LM 209 and phenothiazine shows the importance of the quinuclidine N substitution on the phenothiazine ring, and results in a greater affinity to subcellular particulate fractions (nuclei, mitochondria microsomes). 14 references. (Author abstract modified)

002393 Van Zwieten-Boot, Barbara J.; Petri-Bot, Annelies. Department of Pharmacology, University of Leiden, P.O. Box 722, Leiden, The Netherlands **Absence of a 'cholinergic link' in the apomorphine-induced feedback inhibition of dopamine synthesis in rat striatum.** European Journal of Pharmacology (Amsterdam). 39(2):245-250, 1976.

The effects of cholinergic drugs on the intrastriatal feedback inhibition of dopamine (DA) snythesis were assessed in order to verify the hypothesis that this mechanism is mediated via an intrastriatal cholinergic link. It was presumed that DA receptors were located on a cholinergic neuron while the cholinergic terminals made direct or indirect axon/axonal contact with the dopaminergic nigrostriatal pathway. Although cholinergic agents could modify the effect of 1-hydroxy-3-amino-pyrrolidone-2 on striatal DA content, it was impossible to counteract the blocking effect of apomorphine with cholinergic drugs. It is concluded that the effect of apomorphine is not brought about in the way that had been postulated. 14 references. (Author abstract modified)

002394 Veselkin, N. P.; Kratskin, I. L.; Kasimov, R. Yu.; Palatnikov, G. M. Institut Evolyutsionnoy Fiziologii i Biokhimii im. I. M. Sechenova AN SSSR, Leningrad, USSR **/Bioelectric reactions to visual stimuli in the brain of the sturgeon Acipenser Guldenstadti./** Elektricheskiye reaktsii na zritel'noye razdrazheniye v mozgu osetra Acipenser Guldenstadti. Zhurnal Evolyutsionnoy Biokhimii i Fiziologii (Leningrad). 12(5):483-484, 1976.

An electrophysiological study examined the boundaries of visual perception in 28 sturgeons immobilized by d-turbocurarine. Responses to optic nerve stimulation were recorded through electrodes in the tectum, mesencephalic tegmentum, thalamus and telecephalon of the sturgeon, demonstrating the similarity between the retino-tectal projections in the sturgeon and other fishes. The effects of cholinergic drugs on tectal responses were also studied, and it is supposed that there is an inbibitory system in the mesencephalic tegmentum.

002395 Vikhlyayev, Yu. I.; Lando, L. I.; Artemenko, G. N.; Krupenina, L. B.; Ul'yanova, O. V.; Azyavchik, A. V. Institut farmakologii AMN SSSR, Moscow, USSR **/Neurochemical aspects of the corrective action of phthoracizine in rats with trifluoperazine induced catalepsy./** Neyrokhimicheskiye aspekty korrektornogo deystviya ftoratsizina pri triftazinovoy katalepsii u krys. Farmakologiya i Toksikologiya (Moskva). 39(4):407-411, 1976.

Phthoracizine and trifluoperazine were injected into rats and a comparison was made between the degree of catalepsy and the content of dopamine, noradrenaline, free and bound acetylcholine, and also the activity of cholinesterase in the caudate nuclei and frontal zone of the cortex. Preparations were injected singly or over a period of 8 days. In combined treatment, phthoracizine was injected 30 minutes before trifluoperazine. Phthoracizine lowered the intensity of catalepsy induced by trifluoperazine and normalized the lowered level of dopamine, the higher level of acetylcholine, as well as the activity of cholinesterase. 19 references.

002396 Villeneuve, A. no address **Lithium in psychiatry: a synopsis.** Quebec, Les Presses de l'Universite Laval, 1976. 205 p. $10.

Clinically oriented papers on lithium in psychiatry, which represent the proceedings of the First Canadian International Symposium on Lithium held in May 1974, are presented. The use of lithium in a wide variety of seemingly unrelated psychiatric and nonpsychiatric illnesses are discussed. The findings of a cooperative international study on the course of unipolar depressions and bipolar psychoses are summarized. The psychological problems of lithium use and the instruction of patients, nurses, and primary care physicians on the use of lithium are reviewed.

002397 Warwick, Robert Orem, Jr. Purdue University **The influence of morphine on the kinetics of 3H-serotonin uptake by synaptosomes prepared from rat hypothalamus. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-20296 HC$15.00 MF$8.50 171 p.

Experiments to investigate whether or not there is an association between the acute and chronic actions of morphine on thermoregulation in the rat and the morphine induced alterations in the reuptake of serotonin (5-HT) by hypothalamic nerve endings were conducted. The kinetics of in vitro 3H-5-HT uptake were studied in synaptosomes prepared from the rat hypothalamus. Results indicated that the acute or chronic actions of morphine on rat thermoregulation are not associated with an action of morphine on the 5-HT reuptake mechanism in hypothalamic nerve endings. These conclusions are based on observations of thermoregulatory behavior in rats previously challenged with morphine sulfate and in Ss rendered tolerant to the hypothermic action of the drug. (Journal abstract modified)

002398 Watanabe, Hiroshi Y.; Watanabe, Kazuo. Department of Pharmacometrics, Research Institute for Wakan-yaku, Toyama University, Toyama 930, Japan **Changes in serotonin metabolism of the rat brain and gastric ulceration following water-immersion stress.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):53P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study of the role of the ascending serotonergic nervous system in the perception of exogenous stimuli and adaptation responses in stress situation of rats was reported. The course of changes in serotonin (5-hydroxytryptamine, 5-HT) metabolism and effects of centrally acting drugs were explored in animals with gastric ulceration induced by water immersion stress. Plasma corticosterone increased to 4 times the level seen in unhandled controls. Physical stress induced ulceration was observed in some animals after 1 hr and in all animals after 5 hr. In the brainstem, 5-HT content significantly increased and remained elevated until 8 hr. The levels of 5-hydroxyindoleacetic acid (5-HIAA) in forebrain and brainstem increased in 1 hr and decreased to the level of the unhandled controls at 8 hr. Imipramine, a 5-HT uptake inhibitor, prevented an increase in the forebrain 5-HT level but not in brainstem 5-HT level after 1 hr. Imipramine and desipramine prevented an increase in 5-HIAA content in the forebrain and brainstem after 5 hr stress. Stress ulceration at 5 hr was inhibited by imipramine, desipramine and morphine but not by diazepam and chlordiazepoxide. It is suggested that both 5-HT synthesis and the 5-HT uptake mechanism are activated in the forebrain 5-HT nerve endings and 5-HT synthesis is increased in the brainstem under early stages of physical stress. (Author abstract modified)

002399 Watanabe, Shigenori; Oishi, Ryozo; Ohmori, Kenji; Ueki, Showa. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Kyushu University, Fukuoka 812, Japan **Effect of stimulation of locus coeruleus on electrical activity of the amygdala in rats.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):96P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study of the effects of conditioning stimulation of locus coeruleus (LC) on the evoked potential in the medial amygdala (AME) elicited by electrical stimulation of the olfactory bulb (OB) of the rat was reported. The OB stimulation usually produced a positive potential followed by a negative potential in the AME. Increasing the stimulus frequency resulted in a decrease in amplitude of the negative potential. The amplitude of this potential was inhibited by about 30% by the conditioning stimuli given prior to OB stimulation. The LC inhibitory effect was not changed by phentolamine but was inhibited by propranolol. Methamphetamine showed a biphasic action on the LC inhibitory effect; i.e.,potentiation followed by inhibition. An electrolytic lesion of the dorsal bundle diminished the LC inhibitory effect. The results indicate that the LC may play an inhibitory role in the electrical activity of the AME. (Author abstract modified)

002400 Weinstock, Marta. Department of Physiology and Pharmacology, Sackler School of Medicine, Tel Aviv University, Ramat Aviv, Israel **The presynaptic effect of beta-adrenoceptor antagonists on noradrenergic neurones.** Life Sciences (Oxford). 19(10):1453-1566, 1976.

Studies on the presynaptic effect of propranolol and related drugs on noradrenergic neurons are summarized and mechanisms of action are discussed. Differences reported from in vitro studies are attributed in part to different concentrations of blocking agents: these include studies with rabbits, guinea pigs, and rats. A review of in vivo studies, including those with cats, dogs, and rats, suggests that the ideal beta-adrenoceptor antagonist to use to demonstrate an inhibitory effect on noradrenaline release is one which lacks membrane stabilizing properties and therefore would also be unlikely to inhibit uptake of the release noradrenaline into sympathetic neurons. Mechanisms by which propranolol could reduce the release of noradrenaline, inhibit vascular responses to sympathetic nerve stimulation and reduce the effects of indirectly acting sympathomimetic amines are discussed. Other studies are reviewed which deal with the possible relevance of a presynaptic action to antiarrhythmic, antihypertensive and antipsychotic effects of propranolol and related drugs. 106 references.

002401 Weissman, B. A. Aba Khoushy School of Medicine, Haifa, Israel **Potentiation of dopamine-coupled cyclic AMP generating system in the male rat hypothalamus.** Israel Journal of Medical Sciences (Jerusalem). 12(12):1518, 1976.

A summary of a paper delivered at the 35th meeting of the Israel Physiological and Pharmacological Society on potentiation of dopamine coupled cyclic AMP generating system in the male rat hypothalamus is presented. The combined effects of dopamine and the synthetic estrogen, diethylstilbestrol (DES) on the cAMP generating system was studied. Addition of either one to an incubation medium containing varying concentrations of the other resulted in a synergistic response. It is proposed that DES not only acts as an estrogen by releasing dopamine from nerve terminals, but also by sensitizing the dopamine receptors and thus potentiating the dopamine release.

002402 Wever, K.; Bielicki, L.; Krieglstein, J. Institut fur Pharmakologie im Fachbereich Pharmazie der Philipps-Univer-

sitat, Deutschhausstrasse 17a, D-3550 Marburg/L, Germany **Solubilization of brain mitochondrial hexokinase in anesthesia.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 294(Supplement):R13, 1976.

In a paper presented at a pharmacology meeting in Hannover, Germany, September 14-17, 1976, an attempt to generalize thiopental inhibition of glucose phosphorylation in rat brain by the solubilization of the more active hexokinase form that is bound to the outer mitochondrial membrane is discussed in terms of general anesthesia. The following anesthetics were administered to Sprague-Dawley rats: phenobarbital, hexobarbital, chloral hydrate, ketamine, urethan, halothane, and ether. The cerebral hexokinase activity was determined in a soluble and a mitochondrial fraction. Every drug administered produced a significant increase of hexokinase activity in the soluble fraction. It was concluded that there is a connection between drug induced anesthesia and cerebral hexokinase activity. (Author abstract modified)

002403 Whishaw, Ian Q.; Robinson, Terry E.; Schallert, Timothy. Department of Psychology, University of Lethbridge, Lethbridge, Alberta T1K 3M4, Canada **Intraventricular anti-cholinergics do not block cholinergic hippocampal RSA or neocortical desynchronization in the rabbit or rat.** Pharmacology Biochemistry and Behavior. 5(3):275-283, 1976.

The effects of systemically administered or intraventricularly administered anticholinergic drugs (atropine and scopolamine) on cholinergic hippocampal rhythmical slow activity (theta rhythm, RS) and on neocortical desynchronization were studied in rats and rabbits. Systemic injections, but not intraventricular injections, blocked sensory stimulation induced or eserine induced neocortical desynchronization and hippocampal RSA in rats and rabbits which were immobile and either undrugged or ethanol intoxicated. Systemic injections blocked hippocampal RSA but not neocortical desynchronization in anesthetized rats given sensory stimulation. Intraventricular injections only reduced RSA amplitude in these animals. Neither systemic nor intraventricular injections blocked neocortical desynchronization or hippocampal RSA in animals walking in a motor driven wheel. The hypothesis that there are two types of neocortical desynchronization and hippocampal RSA, one cholinergic and one noncholinergic, is supported. It is also suggested that atropine and scopolamine pass more readily to the neural system responsible for cholinergic electroencephalogram (EEG) activity from the capillary bed than from the ventricular fluid. 34 references. (Author abstract modified)

002404 Wilson, Raymond S.; May, Everette L.; Martin, Billy R.; Dewey, William L. Laboratory of Chemistry, National Institute of Arthritis, Metabolism, and Digestive Diseases, NIH, Bethesda, MD 20014 **9-nor-9-hydroxyhexahydrocannabinols. Synthesis, some behavioral and analgesic properties, and comparison with the tetrahydrocannabinols.** Journal of Medicinal Chemistry. 19(9):1165-1167, 1976.

The synthesis, analgesic properties in mice, some behavioral effects in dogs and mice of the 9-nor-9-hydroxyhexahydrocannabinols, and comparison of these effects with naturally occurring tetrahydrocannabinols are described. Both alpha and beta-hydroxy compounds were active in the dog ataxia test and depressed spontaneous activity in mice. Only the beta-hydroxy compound was an analgesic in mice with morphine like potency. It is suggested that the behavioral and analgesic properties of these compounds is mediated through different sites or mechanisms and is, therefore, separable. 16 references. (Author abstract modified)

002405 Winoukur, Andrew. University of Pennsylvania, Philadelphia, PA 19104 **The distribution and properties of thyrotropin-releasing hormone in hypothalamic and brain tissue. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-22801 HC$15.00 MF$8.50 117 p.

The physiochemical properties of thyrotropin releasing hormone (TRH) were studied from rat brain tissue identified by Bassiri and Utiger's improved radioimmunoassay technique, and the effects of neurotransmitter altering drugs were assessed. Focus was on dose/response curves, inactivation of brain extracts by serum, elution patterns on Septhadex G-25 column, and stimulation of thyrotropin secretion in an in vitro pituitary incubation system. General findings indicated that: 1) TRH is widely distributed throughout rat brain tissue, with only 30% of total brain TRH being in the hypothalamus; 2) none of the drugs that were used or the endocrine manipulations altered TRH distribution; 3) brain TRH was similar to hypothalamic and synthetic TRH; 4) in subcellular fractionation studies, TRH was associated primarily with particulate material and was recovered in highest amounts from the crude mitochondrial fraction, followed by the synaptosomal fraction; 5) after exposure of the crude mitochondrial faction to osmotic shock, the highest concentration was recovered in the synaptic vesicle fraction; 6) TRH is stored in synaptic vesicles, with the microsomal fraction containing the highest concentration of TRH inactivating activity; and 7) administered iontophoretically to hypothalamic neurons, TRH altered the neuronal firing patterns in four of eight cells examined. Findings indicated that TRH may be a CNS neurotransmitter agent. (Journal abstract modified)

002406 Yagi, Fumio. Sophia University, Tokyo, Japan **The effect of parasympathetic and sympathetic interceptors on instrumentally conditioned heartbeat (white rats).** Annual of Animal Psychology (Tokyo). 26(1):49, 1976.

In a paper read to the 36th Symposium of Japanese Animal Psychologists held in June 1976 at Osaka University, the results of an experiment with sympathetic and parasympathetic interceptors on the conditioned acceleration or deceleration of heartrate in white rats are reported to make clear the mechanics of the heartbeat avoidance reaction. Electrical stimulation was used to shape heartbeat over 100 trials/day, and afterward varying doses of atropine sulfate, atropine methylnitrate, propranolol, and phentolamine were administered to the rats. Increased or decreased heartrates were erased by administration of propranolol and atropine. This effect was thought to be due to the temporal interference in the parasympathetic and sympathetic nerve cells which regulate muscular tension in the heart.

002407 Yajima, Takashi; Nakamura, Keiji. Department of Pharmacology, Nippon Roche Research Center, Kamakura 247, Japan **Effects of posterior hypothalamic stimulation on multiple-unit discharges at the baroreceptor-sensitive nucleus tractus solitarius of cats.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):97P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March 1976, a study of the interaction between the baroreceptor afferent and posterior hypothalamic (PHT) pressor activity at the barosensitive nucleus tractus solitarius (NTS) of the medulla oblongata of the cat was reported. Multiunit potentials were discharged constantly at NTS. Pentobarbital abolished the discharges and stabilized the evoked potentials at NTS. Carotid sinus nucleus (CSN) stimulation or norepinephrine (NE) administration mar-

kedly enhanced the density of spontaneous multiunit discharges at NTS. The enhanced discharges at NTS after CSN stimulation were greatly decreased by the subthreshold stimulation of pressor PHT area. The effects of conditioning stimulation of the pressor PHT applied at various intervals on the evoked potentials recorded at the NTS sites following CSN stimulation were also studied. There was a marked reduction in the evoked potentials at NTS by a conditioning stimulation of pressor PHT. The reduction was also abolished by pentobarbital. It is suggested that the pressor area in the posterior hypothalamus may be involved in inhibitory regulation of baroreceptor afferent reception at NTS. (Author abstract modified)

002408 Yanagisawa, Mitsuhiko; Bando, Takeo. Department of Pharmacology, School of Medicine, Juntendo University, Tokyo 113, Japan **Fundamental microquantitative studies by fluorohistochemical method on fluorescence of the monoaminergic neurons in rat brain.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):103P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March 1976, a microquantitative study which employed a fluorohistochemical method of measuring the fluorescence in serotoninergic (5-hydroxytryptamine, 5-HT) neurons of the rat brain was reported. Using a microscopephotometer with a xenon lamp, it was demonstrated that: 1) fluorescence is increased with increasing concentrations of 5-HT but is decreased with high concentrations of 5-HT; 2) fluorescence in most cells is substantially decreased after administration of 40/80 to the rat; 3) fluorescence in raphe nuclei is substantially increased in reserpine and nialamide treated rats; 4) fluorescence of 5-HT cells in the B7 or B8 group is doubled after administration of thiopental; and 5) fluorescence in 5-HT terminals in the suprachiasmatic nuclei increases significantly after administration of nialamide to thiopental pretreated animals. It is concluded that the technique is useful in measuring the fluorescence of 5-HT neurons in the rat brain. (Author abstract modified)

002409 Yehuda, S. Laboratory of Psychopharmacology, Department of Psychology, Bar-Ilan University, Ramat Gan, Israel **Brain dopamine, d-amphetamine and thermoregulation in rats.** Israel Journal of Medical Sciences (Jerusalem). 12(9):1063-1064, 1976.

In a paper from the Jerusalem Satellite Symposium on Temperature Regulation, 1974, the role and effects of brain dopamine (DA) and d-amphetamine on thermoregulation were studied in rats. Previous studies showed that administration of d-amphetamine to rats caused changes in both behavioral and autonomic mechanisms for thermoregulation, suggesting that the hypothermic effect of d-amphetamine may be mediated by the release of brain DA. Subsequent experiments showed that drugs that increase the availability of DA or stimulate DA central receptors (e.g.,apomorphine, clonodine, or ET-495) cause hypothermia, while drugs that decrease DA availability or block interaction between DA and its receptors (e.g.,pimozide, haloperidol, N-ethyl-3-piperidyl phenyl-cyclopentylglycolate, or 6-hydroxydopamine) failed to produce hypothermia and blocked the hypothermic effect of amphetamine. Furthermore, paradoxical behavioral thermoregulation induced by amphetamine was enhanced by DA stimulants and by noradrenaline receptor blockers. Hypothermia and paradoxical behavioral thermoregulation were also blocked in rats with a lesion of the olfactory tubercules, further involving central DA neurons in the role of mediating the thermal effect of amphetamine. It is concluded that DA mediation is an essential role in thermoregulation. 6 references.

002410 Yogi, Hideaki; Inoue, Goen; Tanabe, Kyoko; Kimishima, Kenjiro. Department of Pharmacology, Tottori University School of Medicine, Yonago 683, Japan **Central nervous actions of carbamazepine.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):94P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March 1976, a study of the effects of carbamazepine on behavioral responses induced by methamphetamine and tetrabenazine, on conditioned avoidance responding, on electroshock induced convulsions and drug induced convulsions, and on electroencephalogram (EEG) in mice and rabbits was reported. Following intraperitoneal injection of carbamazepine, locomotor activity was reduced. Chronic administration of carbamazepine for 1 to 3 weeks slightly reduced the locomotor hyperactivity induced by methamphetamine or tetrabenazine. Conditioned avoidance responses in mice were inhibited by the drug. Carbamazepine demonstrated potent anticonvulsant effects against electroshock induced seizures but not against pentetrazol induced convulsions. Following carbamazepine injection, recording of spontaneous EEG activity showed slow waves with high amplitudes in the neocortex. Seizure discharges induced by stimulation of the dorsal hippocampus or amygdala were inhibited, but the arousal response induced by stimulation of the midbrain reticular formation was not. (Author abstract modified)

002411 Yoneda, Yukio; Takashima, Sumie; Kuriyama, Kinya. Department of Pharmacology, Kyoto Prefectural University of Medicine, Kamikyo-Ku, Kyoto 602, Japan **Possible involvement of GABA in morphine analgesia.** Biochemical Pharmacology (Oxford). 25(23):2669-2670, 1976.

The possible involvement of gamma-aminobutyric acid (GABA) in the analgesic action of morphine was studied in STD-ddy mice weighing 23 to 26gm. Analgesic responses were measured by a tail pinch method. Mice were pretreated with either saline 1 hr before the test drug, aminooxyacetic acid 1 hr before, semicarbazide 5 hr before, or bicuculline simultaneously with the test drug. The test drugs were either morphine or aminopyrine. All drugs were given i.p. The threshold for pain was determined every 30 min for 3 hr. GABA levels in the brain were determined fluorometrically after extraction with 75% ethanol. Aminooxyacetic acid significantly prolonged morphine induced analgesic responses, whereas semicarbazide and bicuculline strongly attenuated the morphine analgesia, the effects being most marked at 1 hr. None of the pretreating drugs modified the analgesic effect of aminopyrine. GABA levels in the brain 1 hr after morphine administration were increased 180% in mice pretreated with aminooxyacetic acid and decreased 32% in the mice pretreated with semicarbazide; they were unaffected by bicuculline. Thus, alteration in the GABA content of the CNS may be an important factor for the occurrence of the analgesic action of morphine. 14 references.

002412 Zaks, A. S.; Bykova, A. A.; Ponomareva, S. I. Tsentral'naya nauchno-issledovatel'skaya laboratoriya, Permskogo meditsinskogo instituta, Perm, USSR /**Bioneutralizing properties of serotonin antibodies.**/ O bioneytralizuyushchikh svoystvakh antitel k serotoninu. Farmakologiya i Toksikalogiya (Moskva). 39(6):675-678, 1976.

Although previous research has established that serotonin/protein conjugates evoke the formation of antiserotonin antibodies, the biological role of these antibodies has not been studied, especially in regard to their action on the

effect and metabolic fate of exogenous and endogenous serotonin in vitro or in vivo. Experiments conducted with rabbits demonstrated the formation of antiserotonin antibodies in response to introduction in vivo of a serotonin/protein conjugate. The effect of antibodies on the development of a serotonin induced and dextran induced inflammation in rats and on the serotonin level in cells or organ slices, as well as in the blood thrombocytes, was studied. The antibodies were found to produce an antiphlogistic effect in regard to exogenous and endogenous serotonin. Histochemical investigations showed the antibodies to exert a neutralizing action on intracellular serotonin. 8 references.

002413 Zamir, N.; Gutman, Y.; Ben-Ishay, D. Hebrew University, Hadassah Medical School, Jerusalem, Israel **Hypertension and catecholamine distribution in different parts of the rat brain.** Israel Journal of Medical Sciences (Jerusalem). 12(12):1528, 1976.

A summary of a paper delivered to the 36th meeting of the Israel Physiological and Pharmacological Society on hypertension and catecholamine distribution in different parts of the rat brain is presented. The distribution of the catecholamines, dopamine (DA) and noradrenaline (NA) in different parts of the rat brain in control animals and following induction of hypertension by various methods was examined. The methods by which hypertension was induced and the specific results for each of the three methods are cited. It is suggested that increased NA in the medulla oblongata represents a defense mechanism against the development of hypertension rather than a cause of hypertension.

002414 Zatz, Martin; O'Dea, Robert F. Pharmacology, Laboratory of Clinical Science, NIMH, 9000 Rockville Pike, Bethesda, MD 20014 **Regulation of the protein kinase in rat pineal: increased Vmax in supersensitive glands. (Unpublished paper).** Bethesda, MD, NIMH, 1976. 13 p.

To investigate the regulatory mechanism of protein kinase in rat pineal glands, a series of studies were undertaken. Protein kinase activity was examined in supernatants from supersensitive and subsensitive rat pineal glands, both in the presence and absence of added cAMP. After a 20 min exposure to l-isoproterenol, in vivo or in organ culture, supersensitive pineals displayed a greater increase in protein kinase activity (in the absence of added cAMP) than did subsensitive glands. Furthermore, exposure of rats to 24 h light, a procedure which produces a supersensitive response to beta-adrenergic stimulation, results in a 50% increase in protein kinase activity (with or without added cAMP) as compared to the activity in pineals obtained after 12 h darkness, when the glands are subsensitive. Kinetic analysis revealed a 50 to 100% increase in the Vmax for adenosine triphosphate, histone, and cAMP. This increase in protein kinase was not prevented by prior treatment of rats with cycloheximide. The diminished kinase activity in subsensitive glands did not appear to be due to an increase in the heat stable protein kinase inhibitor. Protein kinase activity also increased after noradrenergic input to the gland was reduced by denervation or depletion of neurotransmitter. Thus, pineal protein kinase may participate in the effects of beta-adrenergic agonists (e.g. the induction of serotonin N-acetyltransferase) and in the regulation of the sensitivity of the gland to beta-adrenergic stimulation. 45 references. (Author abstract)

04 MECHANISM OF ACTION: BEHAVIORAL

002415 Agudelo, Rosa; Ardila, Ruben; Guerrero, Juan. Departamento de Psicologia, Universidad Nacional de Colombia, Bogota, Colombia **/Effects of carbonate of lithium on performance under a program of multiple reinforcement IV 19" RV7.** Efectos del carbonato de litio sobre la ejecucion, bajo un programa de refuerzo multiple, IV 19" RV7. Revista Latinoamericana de Psicologia (Bogota). 8(2):199-236, 1976.

The relatively new concept of behavioral pharmacology of Thompson, Pickens and Marsh is employed in a study to investigate the behavioral effects of lithium carbonate in a reinforcement program. Two albino male rats were employed as subjects and one, as closely identical as possible, was used as a control. The subjects were trained per a multiple IV 19" RV7 program, including an initial stabilization period to establish a baseline. Lithium was administered in doses of 5, 10, 20, and 40mg/kg. In assigned tasks, the subject rats demonstrated a suppression of hyperactivity in direct proportion to the dosage level of lithium carbonate used. It is concluded that it is the combination of method and drug which led to the results observed, and that neither method nor drug should be considered separately when evaluating the results. 115 references.

002416 Allweis, C.; Frieder, B. Hebrew University-Hadassah Medical School, Jerusalem, Israel **Delay of onset of transient amnesia after hypoxia.** Israel Journal of Medical Sciences (Jerusalem). 12(12):1514-1515, 1976.

A summary of a paper which was given on delay of onset of transient amnesia after hypoxia at the 35th meeting of the Israel Physiological and Pharmacological Society is presented. Results of experiments indicated that hypoxia does not abolish short-term memory, but only prevents its transcription to the next holding mechanism, medium term memory. To determine whether the spontaneous return of memory after hypoxia was dependent on RNA synthesis, rats received an intracisternal injection of diaminopurine (DAP), which was timed to prevent long-term memory formation in normal animals. When these animals were subjected to hypoxia immediately after training, memory failed to reappear. When this experiment was repeated with the DAP injection timed to have its effect after the spontaneous reappearance of memory, memory was unaffected.

002417 Anand, M.; Gupta, G. P.; Bhargava, K. P. Industrial Toxicology Research Centre, Post Box No. 80, Lucknow, U.P., India **Effect of tryptaminergic drugs on electroshock fighting behaviour in rats.** European Journal of Pharmacology (Amsterdam). 39(2):389-391, 1976.

The effect of some tryptaminergic drugs on electroshock fighting behavior in rats was determined. Reserpine and tetrabenazine reduced the fighting responses while 5-hydroxytryptophan increased the fighting responses in normal as well as reserpine treated animals. p-Chlorophenylalanine, a specific depletor of brain serotonin, also reduced the fighting responses. It is concluded that an increase of brain serotonin may have a facilitatory effect on electroshock fighting behavior and a decrease of brain serotonin may impair fighting behavior. 12 references. (Author abstract)

002418 Antkiewicz-Michaluk, L. Institute of Pharmacology, Polish Academy of Sciences, 12 Smetna Str., 31-344 Krakow, Poland **Dopaminergic and serotonergic action of ergometrine.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 294(Supplement):R16, 1976.

In a paper presented at a pharmacology meeting in Hannover, Germany, on September 14-17, 1976, the dopaminergic and serotonergic action of ergometrine in meice and rats was

described. Ergometrine (EGM) antagonizes catalepsy induced by butyrophenone neuroleptics, and reserpine syndrome, i.e. catalepsy, ptosis, hypothermia, when given at doses of 5 to 10mg/kg. These doses slightly depress the locomotor activity of normal rats and mice, but they counteract neuroleptic induced locomotor depression. EGM stimulates the hindlimb flexor reflex of spinal rat and inhibits the accumulation of serotonin in the brainstem of pargyline pretreated rats. It was concluded that EGM stimulates both dopaminergic and serotonergic receptors in the brain, the former action being more pronounced after intracerebroventricular injection of EGM. (Author abstract modified)

002419 Ashkenazi, R.; Weinstock, M. Hebrew University, Hadassah Medical School, Jerusalem, Israel **Behavioral effects of paramethoxyphenylethylamine: a pharmacological study.** Israel Journal of Medical Sciences (Jerusalem). 12(12):1518, 1976.

A summary of a paper delivered at the 35th meeting of the Israel Physiological and Pharmacological Society on the behavioral effects of paramethoxyphenylethylamine (PMPEA) is presented. The effects of some drugs on the behavioral response to a dose of 100mg/kg PMPEA s.c. in mice were studied. The experiments indicated that the effect of PMPEA is an indirect one, due to release of biogenic amines in the central nervous system. It also seemed that although catecholamines are involved in the behavioral response, 5-hydroxytryptamine is necessary to initiate it.

002420 Assaf, S. Y.; Mogenson, G. J. Department of Physiology, University of Western Ontario, London, Ontario, Canada **Evidence that the preoptic region is a receptive site for the dipsogenic effects of angiotensin II.** Pharmacology Biochemistry and Behavior. 5(6):697-699, 1976.

To determine if the preoptic area might be a receptive site for the dipsogenic effects of Angiotensin II (ANG II), Ang II was administered to male rats through cannulae passing through the lateral ventricles into the preoptic region. Drinking was attenuated significantly when the ventricles or subfornical organ were pretreated with saralasin acetate (Sar1-Ala8-angiotensin II). If the cannulae in the preoptic region were angled to bypass the lateral ventricles, water intake elicited by ANG II was less and pretreating the cerebral ventricles with saralasin acetate did not reduce the drinking response. The results suggest that the preoptic region may be a receptive site for ANG II in addition to the subfornical organ and/or cerebral ventricles. 15 references. (Author abstract modified)

002421 Babcock, Debra A.; Narver, Ellen L.; Dement, William C.; Mitler, Merrill M. Sleep Laboratory, Dept. of Psychiatry, Stanford University School of Medicine, Stanford, CA 94305 **Effects of imipramine, chlorimipramine, and fluoxetine on cataplexy in dogs.** Pharmacology Biochemistry and Behavior. 5(6):599-602, 1976.

To elucidate the possible role of serotonin uptake blockade in the control of cataplexy, 4 narcoleptic dogs with cataplexy were given trials with the serotonin uptake blockers imipramine and chlorimipramine (known to be effective in treating cataplexy in humans) and the more selective serotonin uptake blocker, fluoxetine. Injections of placebo, test compound, and placebo were given respectively on 3 successive days. Anticataplectic effects were measured approximately 30 min, 3 hr, and 6 hr postinjection by recording elapsed time and number of cataplectic epsiodes during the dogs' attempts to eat ten pieces of a desired food presented in a standard fashion. Imipramine (1mg/kg) and fluoxetine (1.5and 3.0mg/kg) significantly improved performance, while chlorimipramine (0.5-5mg/kg) had no clear effect. Data were not totally consistent with the notion that serotonin uptake blockers improve cataplexy in dogs, since chlorimipramine was not effective in these animals. 18 references. (Author abstract)

002422 Barrett, James E.; Witkin, Jeffrey M. Department of Psychology, University of Maryland, College Park, MD 20742 **Interaction of d-amphetamine with pentobarbital and chlordiazepoxide: effects on punished and unpunished behavior of pigeons.** Pharmacology Biochemistry and Behavior. 5(3):285-292, 1976.

The interaction of d-amphetamine with pentobarbital or chlordiazepoxide and their effects on punished and unpunished behavior in pigeons was studied. Amphetamine alone had no significant effects on overall rates of punished responding. Unpunished responding was either increased slightly or decreased. Pentobarbital and chlordiazepoxide administered alone increased both punished responding and unpunished responding at most doses. Combinations of amphetamine with pentobarbital or chlordiazepoxide produced effects on both punished and unpunished responding that differed substantially from those obtained when any of the drugs were administered separately. Combinations of d-amphetamine with either pentobarbital or chlordiazepoxide produced increases in punished responding that exceeded those obtained with either drug alone, the effects on unpunished responding depended on the individual dose combinations. 21 references. (Author abstract modified)

002423 Beaton, J. M. Department of Psychiatry, University of Alabama Medical Center, University Station, Birmingham, AL 35294 **The sedative effects of nicotinamide on gerbil wheel-running activity.** Experientia (Basel). 32(8):1036-1037, 1976.

The effect of nicotinamide on wheel running activity was studied in 25 adult, male gerbils weighing 55 to 65g. Baseline measures were taken three times a week for 2 weeks. The gerbils were then divided into five groups: a nontreatment group, and groups receiving saline, and 125mg/kg 250mg/kg nicotinamide i.p. daily. Animals were run in the wheel 30 min after the injection on days 1, 3, 8, 10, 15, 17, and 22. Wheel running sessions lasted 30 min. The 250mg/kg and 500mg/kg doses of nicotinamide decreased wheel running activity. The results suggest that nicotinamide has a central effect unrelated to its role as a vitamin. 7 references.

002424 Berntson, Gary G.; Beattie, Michael S.; Walker, J. Michael. Laboratory of Comparative and Physiological Psychology, Ohio State University, 1314 Kinnear Road, Columbus, OH 43212 **Effects of nicotinic and muscarinic compounds on biting attack in the cat.** Pharmacology Biochemistry and Behavior. 5(3):235-239, 1976.

To further assess the role of cholinergic systems in the control of aggressive behaviors, the effects of nicotinic and muscarinic compounds on aggression in the cat were studied. Biting attack on a rat and other threat behaviors were induced in normally nonaggressive cats by systemic administration of the muscarinic agonist arecoline. Nicotine alone suppressed aggressive behaviors, while systemic administration of nicotine prior to arecoline injection produced a significant reduction in elicited attack and threat behaviors. Nicotine also produced a dose dependent suppression of natural predatory behavior. Nicotine induced suppression of attack did not appear to be due to the induction of general malaise. It is concluded that muscarinic and nicotinic compounds can exert antagonistic control over some types of aggressive behaviors, suggesting

the involvement of a muscarinic cholinergic mechanism controlling predatory behavior in the cat. 32 references. (Author abstract modified)

002425 Bigler, Erin D. Division of Neurobiology, Barrow Neurological Institute, St. Joseph's Hospital, 350 West Thomas Road, Phoenix, AZ 85013 **Diazepam modification of evoked and spontaneous lateral geniculate activity.** Electroencephalography and Clinical Neurophysiology (Amsterdam). 41(4):428-433, 1976.

The effects of diazepam on evoked and spontaneous activity of dorsal lateral geniculate nucleus (dLGN) principal (P) and inhibitory (I) cells were examined in rats. In the majority of P cells tested both spontaneous and evoked activity were suppressed following diazepam treatment with these effects being altered little by a pentylenetetrazol (Metrazol) challenge. I cell spontaneous activity was suppressed by diazepam and augmented by the Metrazol challenge; however, posttimulus activity was relatively unaffected by either treatment. Results were discussed in terms of support for a functional re evaluation of the rat dLGN. 21 references. (Author abstract modified)

002426 Bigler, Erin D.; Eidelberg, Eduardo. Division of Neurobiology, Barrow Neurological Institute of St. Joseph's Hospital and Medical Center, Phoenix, AZ 85013 **Nigrostriatal effects of morphine in two mouse strains.** Life Sciences (Oxford). 19(9):1399-1406, 1976.

The effects of morphine on nigrostriatal neurons (substantia nigra and caudate nucleus) were examined in mice of two strains (C58 and DBA), which differ in their locomotor response to morphine. The results did not support the hypothesis that the differences in locomotor response to morphine between the two strains are paralleled by differences in the response of nigrostriatal neurons to the same drug. The general effect of morphine on nigrostriatal neurons, irrespective of strain, was to markedly depress their firing rate. Some nigrostriatal neurons initially speeded up but this effect was strain independent. This same general pattern was observed in some neurons recorded within the reticular formation. The results are discussed in relationship to the current concepts of morphine action on dopaminergic systems and the role of the nigrostriatal system in locomotor control. 23 references. (Author abstract)

002427 Boissier, J. R.; Simon, P.; Soubrie, P. Unite de Neuropsychopharmacologie de l'INSERM, 2 rue d'Alesia, F-75014 Paris, France **New approaches to the study of anxiety and anxiolytic drugs in animal.** In: Airaksinen, M., CNS and behavioural pharmacology. Elmsford, New York, Pergamon Press, 1976. 344 p. v. 3. (p. 213-222).

In a paper presented at the Sixth International Congress of Pharmacology held in Helsinki, Finland in July, 1975, animal models of anxiety and their use in the study of anxiolytic drugs are discussed. The first model uses an enclosure with a staircase; the number of rearings and number of steps climbed are counted as indices of anxiety and exploration, respectively, of a naive rat placed in the enclosure. Drug studies using this model have revealed that: 1) neuroleptics, antihistaminic drugs, tricyclic antidepressants, sulpiride, ethaphenoxine, muscle relaxants, and antiepileptic drugs induce a parallel decrease in the number of steps climbed and in the number of rearings; 2) anticholinergic drugs induce a decrease in the number of steps climbed at doses which do not modify the number of rearings; and 3) benzodiazepines, barbiturates, and quinazolones decrease rearings at doses which either do not modify or increase the number of steps climbed. Studies using hypophagia induced by exposure of rats and mice to novel foods in a novel environment as a measure of anxiety have revealed that diazepam, chlordiazepoxide, oxazepam, lorazepam, nitrazepam, amobarbital, and meprobamate increase food intake. However, the ability of these drugs to increase hunger drive cannot be ruled out as pertinent to the response. A third model uses drug induced hypermotility to assess the effects of anxioltyic drugs. Studies using this model have revealed that diazepam does not counteract and may increase locomotor hyperactivity induced by amphetamine, cocaine, or morphine; however, in doses that do not modify the spontaneous locomotor activity of the mouse, diazepam decreases hyperactivity induced by trihexyphenidyl or by reserpine in monoamine oxidase inhibitor pretreated animals. Other studies have assessed the action of antianxiety drugs on restraint stress induced ulcers in rats previously assessed as being emotional or nonemotional. The emotional animals develop gastric ulcers more rapidly than do nonemotional animals, diazepam and prazepam protect emotional animals against ulcers in doses which are ineffective in nonemotional animals, whereas imipramine and amphetamine protect both groups equally. Emotional rats are also more inhibited in the heated floor maze than nonemotional rats. It has been found that this behavioral inhibition is almost completely suppressed by diazepam, oxazepam, and amobarbital but is not modified by chlorpromazine, imipramine, amphetamine, or morphine. 37 references.

002428 Borisenko, S. A. Laboratoriya farmakoterapii ekstremal'nykh sostoyaniy Instituta farmakologii AMN SSSR, Moscow, USSR **/Mechanism of analgesic effects of narcotics./** K mekhanizmu boleutolyayushchego deystviya narkoticheskikh anal'getikov. Byulleten' Eksperimental'noy Biologii i Meditsiny (Moskva). 81(4):432-434, 1976.

Effects of morphine, promedol, fentanyl, pentazocine and the psychostimulant fenamine on the threshold of pain sensitivity and self-stimulation of the hypothalamus and the septum were studied in rats. Results show that electrical stimulation of the systems of positive reinforcement of the hypothalamus and the septum together with analgesics increased the threshold, whereas fenamine failed to influence it. Morphine and finamine facilitated, promedol failed to influence, fentanyl decreased and pentazocine completely depressed hypothalamic self-stimulation. Septal self-stimulation was not affected by morphine, promedol and fentanyl but decreased under the effect of pentazocine and increased under fenamine. 15 references.

002429 Boullin, D. J.; Green, A. R. University Department of Clinical Pharmacology, Radcliffe Infirmary, Oxford OX2 6HE, England **5-Methoxytryptamine: stimulation of 5-HT receptors mediating the rat hyperactivity syndrome and blood platelet aggregation.** Advances in Biochemical Psychopharmacology. 15:127-140, 1976.

Studies of the central receptor effects of 5-methoxytryptamine (5-MT) as determined by behavioral changes induced in rats after intraperitoneal (i.p.)injection and of the peripheral receptor effects of 5-MT as determined by human blood platelet aggregation responses are reported. When administered ip without prior treatment with a monoamine oxidase inhibitor (MAOI), 5-MT produced transient behavioral changes lasting 5 to 10 min. No 5-MT was detectable in the brain. After pretreatment with the MAOI tranylcypromine, 5-MT produced dose dependent behavioral changes (hyperactivity) within 5 min after doses of 2.5mg/kg to

50mg/kg, and 5-MT accumulated in the brain with maximum levels being reached after 30mg/kg. The behavioral effects of 5-MT were: 1) mimicked by quipazine, a serotonin (5-hydroxytryptamine, 5-HT) receptor stimulant; 2) attenuated by lysergic acid diethylamide (LSD), a 5-HT antagonist; 3) blocked by haloperidol; 4) unaffected by parachlorophenylalanine; and 5) not mimicked by i.p. injection of melatonin or by i.p. administration of 5-HT (which does not readily enter the brain from the periphery). The evidence suggests that the action of 5-MT is central in origin and probably mediated via an effect on postsynaptic 5-HT receptors or specific 5-MT receptors. 5-MT produced a transient reversible aggregation response in human platelets, similar to that produced by 5-HT. This effect was antagonized by LSD and mimicked by quipazine, confirming that 5-MT acts on 5-HT receptors. It is pointed out that further study is needed to confirm the existence of separate 5-MT receptors and to establish whether or not 5-MT is a neurotransmitter in the brain. 24 references.

002430 Bowen, Florry P. Department of Neurology, Mt. Sinai School of Medicine, New York, NY 10029 **Behavioral alterations in patients with basal ganglia lesions.** In: Yahr, M., The basal ganglia. Vol. 55. New York, Raven Press, 1976. 474 p. (p. 169-180).

In a paper presented at the 55th meeting of the Association for Research in Nervous and Mental Disease, behavioral alterations in patients with basal ganglia lesions were described, based on initial neuropsychological studies of notions that the basal ganglia play a role in regulating proprioceptive and vestibular mechanisms, and on the finding that similar behavioral changes can be seen after frontal lobe and basal ganglia lesions in animals, especially in regard to perceptual motor disturbances. Parkinsonian patients awaiting surgical intervention for relief of rigidity and of tremor symptoms were subjected to a test protocol which indicated their difficulty in adjusting visual/vertical perception and judging postural/vertical perception with vision excluded. Further studies contrasting Parkinsonian patients with cortically damaged patients revealed that on two tasks of spatial orientation, the former Ss also make significantly more errors than matched normal controls, but do not have primary sensory deficits in contrast to the latter Ss. Differential responses suggest hemispheric specialization is affected by basal ganglia lesions. With development of levodopa therapy, additional studies indicate that the main difficulties experienced by Parkinsonian patients is in short-term memory in concept formation and shifting of sets in the absence of primary deficits in the registration of sensory stimuli. Overall findings suggest that Parkinsonian patients have behavioral changes similar to those experienced by patients with postencephalitic processes and those with subcortical dementia. 33 references.

002431 Brailowsky, Simon; Naquet, Robert. Departement de Neurophysiologie Appliquee, Laboratoire de Physiologie Nerveuse du C.N.R.S., F-91190 Gif-sur-Yvette, France **Effects of drugs modifying brain levels of catecholamines on photically induced epilepsy in Papio papio.** Epilepsia (Amsterdam). 17(3):271-274, 1976.

The behavioral and electrographic effects of DL-amphetamine, disulfiram, FLA-63, and propranolol on photically induced epilepsy the Sengalese baboon were evaluated. Amphetamine produced somatic hypokinesia with enhancement of eye movements, diminution of spontaneous paroxysmal activity, and little change in photosensitivity. The acute effects of disulfiram and FLA-63 were poor, but the latter was lethal in the days following administration. Propranolol showed no consistent effects. Participation of catecholamine processes in this type of experimental reflex epilepsy are discussed. It is concluded that systemic administration of drugs which modify brain catecholamine levels do not act clearly on this animal model of human epilepsy. 17 references. (Author abstract)

002432 Burov, Yu. V. Institute of Pharmacology, Academy of Medical Sciences of the USSR, Moscow 125315, USSR **The influence of psychotropic drugs upon emotions.** In: Airaksinen, M., CNS and behavioural pharmacology. Elmsford, New York, Pergamon Press, 1976. 344 p. v. 3. (p. 197-205).

In a paper presented at the Sixth International Congress of Pharmacology held in Helsinki, Finland in July, 1975, a series of studies of the influence of psychotropic drugs upon emotional responses in rats are reported. The effects of neuroleptics (chlorpromazine, trifluoperazine, haloperidol, and droperidol), minor tranquilizers (benactyzine, chlordiazepoxide, and meprobamate), antidepressants (imipramine, ftoracyzine), a psychostimulant (amphetamine), a psychotomimetic drug (LSD), and an analgesic (morphine) on the escape behavior produced in one animal by pain stimulation of another were investigated and compared with their effects on a conditioned defense reflex. Only amphetamine in certain doses failed to inhibit the escape behavior. The doses of drugs required for inhibition of the defense conditioned reflex and for inhibition of the escape behavior were significantly different except for phenothiazine neuroleptics. Benactyzine, meprobamate, and chlordiazepoxide altered the escape reaction in relatively low doses but failed to affect the defense conditioned reflex. Studies of the effects of muscarinic cholinolytics, nicotinic cholinolytics, alpha-adrenoreceptor blocking agents, beta-adrenoreceptor blocking drugs, and serotonergic antagonists indicated that muscarinic cholinergic and alpha-adrenergic structures are involved in the formation and realization of the escape behavior induced in an animal by pain stimulation of another animal. Studies of the effects of various drugs on motivated aggression when two animals were competing to escape electric shock by jumping onto a bench) and nonmotivated aggression (with no escape available) revealed that: 1) pentobarbital and chlorpromazine inhibited both types of aggression in the same doses; 2) antidepressants reduced nonmotivated aggression only; and 3) minor tranquilizers, trifluoperazine, and haloperidol inhibited motivated aggression in much lower doses than nonmotivated aggression. The effectiveness of the minor tranquilizers in reducing intraspecies aggression differs from their ineffectiveness in interspecies aggression. 8 references.

002433 Colpaert, F. C.; Leysen, J. E. M. F.; Niemegeers, C. J. E.; Janssen, P. A. J. Dept. of Pharmacology, Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **Blockade of apomorphine's discriminative stimulus properties: relation to neuroleptic activity in neuropharmacological and biochemical assays.** Pharmacology Biochemistry and Behavior. 5(6):671-679, 1976.

Using a food reinforced two lever operant conditioning procedure, rats were trained to discriminate 0.16mg/kg apomorphine from saline, and 8 neuroleptics of the phenothiazine, butyrophenone, or diphenylbutylamine type were investigated for their ability to antagonize the discriminative stimulus properties of apomorphine. The same drugs were also assayed for in vivo antagonism of apomorphine induced stereotyped behavior as well as for in vitro inhibition of stereospecific 3H-haloperidol binding in rat striatal tissue preparations. The data are consistent with the hypothesis that apomorphine exerts its discriminative stimulus properties by a

mechanism similar to that underlying its stereotypogenic action. It was suggested that the loci involved in these two phenomena are likely to be distinct. 32 references. (Author abstract)

002434 Consroe, Paul; Jones, Byron; Laird, Hugh, II. Department of Pharmacology and Toxicology, College of Pharmacy, University of Arizona, Tucson, AZ 85721 **EEG and behavioral effects of delta9-tetrahydrocannabinol in combination with stimulant drugs in rabbits.** Psychopharmacology (Berlin). 50(1):47-52, 1976.

The electroncephalogram (EEG) and behavioral effect of delta9-tetrahydrocannabinol (THC) were examined in the rabbit in combination with methamphetamine, cocaine, apomorphine, or caffeine. Cortical and hippocampal alterations produced by THC were antagonized by methamphetamine, cocaine, and caffeine and only briefly by apomorphine. Postural activity behaviors were reversed by methamphetamine and caffeine but only briefly by cocaine and apomorphine. Additionally, stereotypy resulted from the combination of THC with methamphetamine, cocaine, or apomorphine. These data indicate that the effects of THC were antagonized by stimulant drugs of which caffeine was the most effective. However, novel toxicity also resulted from the interaction of THC with catecholaminergic drugs. 35 references. (Author abstract modified)

002435 Cook, Leonard; Sepinwall, Jerry. Department of Pharmacology, Research Division, Hoffman-La Roche, Inc, Nutley, NJ 07110 **Animal psychopharmacological procedures: predictive value for drug effects in mental and emotional disorders.** In: Airaksinen, M., CNS and behavioural pharmacology. Elmsford, New York, Pergamon Press, 1976. 344 p. v. 3. (p. 223-235).

In a paper presented at the Sixth International Congress of Pharmacology held in Helsinki, Finland in July, 1975, animal models for assessing the psychotherapeutic effects of neuroleptics, antidepressants, and anxiety agents are discussed with emphasis on the predictive validity of such tests for their usefulness in treating mental and emotional disorders and on the use of such tests to study some hypotheses concerning the pharmacological mechanisms of action of these drugs. Limitations or constraints upon interpretations applied to certain models, such as the conditioned emotional response procedure, are discussed. Specific topics included are: 1) the use of animal conditioned avoidance behavior as an empirical predictor of antipsychotic activity; 2) drug interaction tests, in which the activity measured is antagonism or potentiation of the effects of other drugs; 3) procedures which measure antiaggressive effects such as antagonism of footshock induced fighting; 4) the assessment of drug effects on conflict induced by pairing appetitive and aversive reinforcement; 5) correlation of the antianxiety effects of drugs as measured via the conflict nodel and their abilities to inhibit cyclic adenosine monophosphate phosphodiesterase; 6) correlation of the anticonflict effects of drugs with their glycine receptor affinities as measured by strychnine displacement at glycine receptor sites in rat CNS; 7) investigations of the hypothesis that gamma-aminobutyric acid, serotonin (5-hydroxytryptamine), or norepinephrine (noradrenaline) is involved in the mediation of the antianxiety effects of benzodiazepines; and 8) studies using the conflict model to assess the possible antianxiety effects of the beta-adrenoceptor blocking drug propranolol. 42 references.

002436 Costall, Brenda; Marsden, C. David; Naylor, Robert J.; Pycock, Christopher J. Postgraduate School of Studies in Pharmacology, University of Bradford, Bradford, West Yorkshire, England **The relationship between striatal and mesolimbic dopamine dysfunction and the nature of circling responses following 6-hydroxydopamine and electrolytic lesions of the ascending dopamine systems of rat brain.** Brain Research. 118(1):87-113, 1976.

Adult male rats had 6-hydroxydopamine (6-OHDA) placed in the brain and electrolesions made in cell bodies, axons and terminals to investigate the importance of extrapyramidal and mesolimbic function for circling behavior. Circling behavior was weak when 6-OHDA was placed at the center of the substantia nigra (SN), but the characteristic contralateral/ipsilateral turning to apomorphine/amphetamine were recorded. Circling was more marked when 6-OHDA was placed anterior to the SN but was generally absent following injections posterior to the SN. However, 6-OHDA placed in the medial forebrain bundle in the lateral hypothalamus resulted in intense contralateral/ipsilateral turning to apomorphine/amphetamine. Generally, the intensity of circling responses was related to the degree of striatal dopamine (DA) depletion, but the more effective lesions also caused reductions in mesolimbic DA content. However, circling was not observed following any 6-OHDA injection into the mesolimbic DA system, and it was concluded that mesolimbic DA function is not essential for the initiation of circling. In contrast to the 6-OHDA lesions, rats circled ipsilateral to both apomorphine and amphetamine when the SN was damaged by electrocoagulation to cause marked depletion of striatal dopamine. It is suggested that electrolesions of the SN cause different effect to 6-OHDA because they destroy neuronal pathways in addition to the dopaminergic nigrostriatal tract which appear to be required for the expression of circling behaviour caused by stimulation of the denervated striatum. Whereas 6-OHDA lesions result in supersensitivity of the denervated striatal DA receptors, electrolesions may cause a hyposensitivity of the same receptor sites. 29 references. (Author abstract modified)

002437 Davis, W. Marvin; Smith, Stanley G. Dept. of Pharmacology, University of Mississippi, University, MS 38677 **Role of conditioned reinforcers in the initiation, maintenance and extinction of drug-seeking behavior.** Pavlovian Journal of Biological Science. 11(4):222-236, 1976.

The role of conditioned reinforcers in the initiation, maintenance and extinction of drug seeking behavior was studied in rats to explore further the occurrence and motivational properties of secondary reinforcers derived from the primary reinforcing action of intravenous morphine injections. Secondary reinforcement developed in the absence of physical dependence and followed the association of the stimulus with either response contingent or noncontingent injections of morphine. Strength of the conditioned reinforcer, measured in terms of responding on a lever for the stimulus plus infusion of saline solution, was proportional to the unit dosage of morphine employed in pairings of buzzer and drug. When extinction of the lever press response for morphine was conducted (by substituting saline for morphine solution) in the absence of the conditioned reinforcing stimulus, it was seen later that the stimulus could still elicit lever responses, until it, too, had been present for a sufficient interval of nonreinforced responding. Similarly, extinction of the response for morphine by blocking its action with naloxone in the absence of the stimulus did not eliminate the conditioned reinforcement. Another study showed that a passive, subcultaneous dose of morphine served to maintain lever pressing on a contigency of

buzzer plus saline infusion. Furthermore, the stimuli resulting from the presence of morphine (after an injection) were able to reinstate the lever responding with only the buzzer saline contingency when such responses had previously been extinguished. Moreover, it was shown that d-amphetamine could restore responding under the same conditions, and that morphine could also do so for rats in which the primary reinforcer had been d-amphetamine. It is suggested that animal data such as these show that procedures designed for the elimination of human drug taking behavior must take into account secondary reinforcers as well as the primary reinforcer. 21 references. (Author abstract modified)

002438 Di Chiara, G.; Porceddu, M. L.; Vargiu, L.; Argiolas, A.; Gessa, G. L. Institute of Pharmacology, University of Cagliari, Via Porcell, 4, I-09199 Cagliari, Italy **Evidence for dopamine receptors mediating sedation in the mouse brain.** Nature (London). 264(5586):564-567, 1976.

The mediation of sedation by dopamine receptors (DA) in the mouse brain was investigated. Neuroleptics such as haloperidol, droperidol, pimozide, benzperidol, and sulpiride were able to prevent the sedative effect of apomorphine and L-dopa and also the ability of apomorphine to inhibit the activity of the DA system. These results suggest that apomorphine and L-dopa produce sedation and decrease dopaminergic activity by stimulating central DA receptors. The strict correlation between the behavioral and biochemical changes indicates that the sedative effect of apomorphine probably depends on decreased DA activity. 19 references.

002439 Dolphin, A.; Elliott, P. N. C.; Jenner, P. University Department of Neurology, Institute of Psychiatry, Denmark Hill, London, SE5, England **The irritant properties of dopamine-beta-hydroxylase inhibitors in relation to their effects on L-dopa-induced locomotor activity.** Journal of Pharmacy and Phramacology (London). 28(10):782-785, 1976.

Male mice were administered the dopamine-beta-hydroxylase inhibitors (DBHIs) FLA-63 and U10,157 to investigate their effect on mediation by irritation on L-dopa induced motor activity. FLA-63 and carrageenan were both highly irritant compared to saline. Comparison of irritant properties of kaolin and U10,157 showed no clear increase in irritant potency compared to methycellulose either in the induction of paw edema or in the stimulation of peritoneal exudation. Because inhibition of L-Dopa induced locomotor activity is produced by only FLA-63 and U10,157 and not carrageenan or kaolin, it is suggested that the observed attenuation of L-dopa induced activity does not result from irritant properties of the DBHIs which lends support to the possibility that there is a causal relation between inhibition of DBH by these drugs and observed behavioral effects. 14 references.

002440 Einon, Dorothy; Stewart, Jane; Atkinson, Suzanne; Morgan, Michael. Psychological Laboratory, University of Cambridge, Downing Street, Cambridge CB2 3EB, England **Effect of isolation on barbiturate anaesthesia in the rat.** Psychopharmacology (Berlin). 50(1):85-88, 1976.

The duration of barbiturate induced sleeping in rats was studied during social isolation. It was found that sleeping was reduced by isolation housing. It was also lower in males than females, and lower in the dark phase of the diurnal cyle. These variables were shown to be additive in their effects. Sex differences in barbiturate action were found to be reduced by gonadectomy in males; and the effects of isolation were found to depend upon housing conditions at the time of testing rather than upon early rearing environment. The implication for theories of arousal is discussed. 28 references. (Author abstract)

002441 Eliasson, Mona. Department of Medical Pharmacology, Box 573, S-751 23, Uppsala, Sweden **Actions of repeated injections of LSD and apomorphine on the copulatory response of female rats.** Pharmacology Biochemistry and Behavior. 5(6):621-625, 1976.

Two experiments with female rats were undertaken in order to determine the comparative effects of lysergic acid diethylamide (LSD) and apomorphine on the copulatory responses of female rats, and the development of tolerance to LSD. LSD, a serotonin receptor stimulating agent, inhibits copulatory behavior (lordosis response) in the ovariectomized and estrogen plus progesterone treated female rat. The same effect is obtained by apomorphine, a dopamine receptor stimulating compounds. The lordosis has been shown to be dependent on serotonin, but also dopamine has been implicated in its mediation. Tolerance develops to certain responses after repeated injections of LSD and in the present study the influence of apomorphine and LSD was compared, when given in repeated doses. Possible cross-tolerance between the 2 compounds was also tested on the frequency of lordosis responding in ovariectomized and hormone treated female rats. Tolerance to LSD develops over 7 days, while the suppressing influence of apomorphine on lordosis in 7 repeated doses is not significantly altered from that of a single dose. No cross-tolerance was observed on the lordosis response with either order of treatments. Repeated doses of LSD did not influence locomotor activity differently from a single dose, while repeated doses of apomorphine enhanced this response in comparison with the effect of an acute dose. These results indicate differential sensitivity to the repeated treatments and further support an interpretation of the LSD effects on lordosis responding to be primarily on serotonergic rather than dopaminergic receptors. 32 references. (Author abstract modified)

002442 Engel, Jorgen; Liljequist, Sture. Department of Pharmacology, University of Goteborg, Fack, S-400 33 Goteborg, Sweden **Behavioural effects of beta-receptor blocking agents in experimental animals.** In: Carlsson, C., Neuro-psychiatric effects of adrenergic beta-receptor. Munich, Urban & Schwarzenburg, 1976. 120 p. (p. 45-52).

In a paper presented at a symposium on neuropsychiatric effects of adrenergic beta-receptor blocking agents held in Copenhagen, October 1975, it is reported that female mice of the N.M.R.I. strain were used in a series of experiments which attempted to consider the various pharmacological effects of beta-receptor blocking agents when investigating possible central effects. Results were found with respect to membrane stabilizing activity, central versus peripheral effects, and the relative importance of beta1 and/or beta2 receptors. Taken together, the results of the series of experiments are seen as suggesting that central beta-receptor mechanisms may be involved in the suppressive effect of dl-propranolol on locomotor stimulation which was observed after administration of ethanol. Whether these receptor mechanisms belong to dopamine, noradrenaline, adrenaline, or other neurotransmitter systems in the brain remains to be clarified. 37 references.

002443 Farber, Philip D.; Gorman, Judith E.; Reid, Larry D. Midwest Institute of Drug Abuse, University of Wisconsin at Milwaukee, Milwaukee, WI 53202 **Morphine injections in the taste aversion paradigm.** Physiological Psychology. 4(3):365-368, 1976.

In three separate studies, rats were presented with a flavored solution and then injected with one of a variety of doses of morphine in the taste aversion paradigm. In one experiment it was demonstrated that injections following the first

five injections still had capabilities of suppressing drinking. It made little difference whether the injections were subcutaneously or intraperitoneally given. There were considerable individual differences with respect to extent of suppression of drinking the flavored solution. Some rats showed almost complete suppression but others only a slight suppression. 13 references. (Author abstract modified)

002444 Farber, Philip D.; Reid, Larry D. Department of Psychology, University of Wisconsin-Milwaukee, Milwaukee, WI 53201 **Addictive agents and intracranial stimulation (ICS): daily morphine and pressing for combinations of positive and negative ICS.** Physiological Psychology. 4(3):262-268, 1976.

Ten rats were fixed with two chronically indwelling bipolar electrodes, stimulation of one producing positive intracranial stimulation (P-ICS) and stimulation of the other producing aversive, or negative, intracranial stimulation (N-ICS). Subjects pressed a lever daily for P-ICS and for combinations of P-ICS and N-ICS. Following baseline measurements, five rats received daily injections of morphine sulfate for 20 days while the other five received placebos. Press rates of the morphine subjects for P-ICS increased about 20% from baseline rates and from rates of rats under placebo some days after injections were begun, and these increases were then maintained throughout the days of injections. For the combined P-ICS and N-ICS, press rates of rats of morphine decreased with continued injections. Because of morphine's differential effects on pressing for P-ICS and on pressing for combinations of P-ICS and N-ICS, it is suggested that facilitatory effect of morphine on hypothalamic self-stimulation is not related to its analgesic properties. 14 references. (Author abstract modified)

002445 Finnegan, Kevin T.; Kanner, Marilyn I.; Meltzer, Herbert Y. Department of Psychiatry, Univ. of Chicago Pritzker School of Medicine, 950 E. 59th St., Chicago, IL 60637 **Phencyclidine-induced rotational behavior in rats with nigrostriatal lesions and its modulation by dopaminergic and cholinergic agents.** Pharmacology Biochemistry and Behavior. 5(6):651-660, 1976.

A series of experiments were undertaken to investigate whether phencyclidine (1-(phenylcyclohexyl) piperidine hydrochloride (PCP) interacts with dopaminergic and cholinergic systems as manifested by turning behavior in the rat. The peripheral administration of PCP induces a dose related ipsilateral rotation in unilateral substantia nigra electrolytically lesioned rats. The intensity of this rotation can be modulated by administration of various dopaminergic and cholinergic agents. Injection of alpha-methylparatyrosine methylester (125mg/kg) or haloperidol (1mg/kg) inhibited the ipsilateral circling behavior. Pimozide (1mg/kg) also inhibited the rotation, but to a lesser extent. The injection of the anticholinergic agent trihexyphenidyl (5mg/kg) potentiated, and the cholinomimetic drug arecoline (5mg/kg), depressed the rotation induced by PCP (7.5mg/kg). It is probable that PCP possesses significant dopaminergic and anticholinergic properties. The capacity of PCP to induce rotation in this model may be related to its effects on dopaminergic and cholingergic neurons in the rat striatum. Thus, PCP may induce rotational behavior by potentiating dopaminergic transmission, by blocking cholinergic activity, or both. Both of these effects have been demonstrated to be important in the generation of circling behavior in rats with nigrostriatal lesions. 75 references. (Author abstract modified)

002446 Fish, Barbara Schneiderman. University of Florida, Gainesville, FL 32611 **Catecholamine modulation of behavior following bilateral hippocampal damage. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. Microfilms, No. 77-1115 HC$15.00 MF$8.50 116 p.

Alterations in behavior produced by pharmacologic manipulations affecting the central catecholamine systems after bilateral hippocampal damage in the rat were studied. Findings indicated that: 1) high doses of amphetamines decreased responding on fixed-ratio (FR) schedules in Ss with hippocampus damage, while norepinephrine (NE) and dopamine (DA) receptor stimulants caused no decrease; 2) data on the blockers of NE and DA synthesis (alpha-methyl-para-tyrosine-AMT), NE synthesis and the postsynaptic DA receptor blocker, haloperidol, indicated that only haloperidol improved deficient DRL-20 performance of hippocampally damaged Ss; 3) AMT and haloperidol decreased the intertrial interval responding of Ss with hippocampus damage performing on a stimultaneous brightness discrimination task; and 4) NE synthesis did not alter performance of any Ss on either the DRL or the discrimination task. Results are discussed in relationship to a functional antagonism between the hippocampus and dopaminergic systems in the mediation of some behaviors. (Journal abstract modified)

002447 Fowler, Stephen C. University of Mississippi, University, MS 38677 **Behavioral drug effects upon operant response force.** Final report, NIMH Grant MH-27177, August, 1976. 13 p.

Rats trained to press a force sensing, nearly isometric manipulator coupled to a force proportional transducer were administered chlorpromazine, chlordiazepoxide, and d-amphetamine to investigate drug influence on operant response measures of peak force, duration, time integral of force, and interresponse time (IRT) using different reenforcement schedules. Results from all completed experiments suggest that the intensitive properties of individual operant responses are reliable dependent measures of behavioral drug effects. Peak force, durateion, and IRT or rate of response proved to be the most valuable variables for characterizing the effects of the various compounds. Time integral of force as a dependent variable provided little information not available from either peak force or the duration measure. In many cases, the force variable provided information unavailable from the rate measure alone. D-amphetamine significantly affected peak force and IRT, but did not reliably influence duration. Significant interaction of force and IRT suggested high rate/high force and low force/low rate components were differentially affected by the drug. Chlordiazepoxide increased peak force and duration while lengthening IRT. A schedule dependence effect was present for the IRT variable. Dantrolene decreased peak force, increased duration, but did not significantly affect IRT. 13 references.

002448 Frontali, Marina; Amorico, Luigi; De Acetis, Luigi; Bignami, Giorgio. Istituto di Psicologia, Consiglio Nazionale delle Ricerche, Via dei Monti Tiburtini 509, Rome I-00157, Italy **A pharmacological analysis of processes underlying differential responding: a review and further experiments with scopolamine, amphetamine, lysergic acid diethylamide (LSD-25), chlordiazepoxide, physostigmine, and chlorpromazine.** Behavioral Biology. 18(1):1-74, 1976.

A pharmacological analysis of processes underlying differential responding in rats to psychotropic agents is presented. The results demonstrate that: 1) enhancements of locomotor responses to no go signals can occur after scopolamine and amphetamine; 2) complex interactions between treatments, cues, and response reinforcement rela-

tions can lead to marked differences between amphetamine and scopolamine hyperresponding; 3) a moderate LSD-25 disinhibition can take place in conditioned inhibition tasks; 4) a moderate disinhibition occurs after chlordiazepoxide treatments; 5) the physostigmine facilitation of differential responding does not depend on the particular response reinforcement contingency; and 6) the chlorpromazine depression of active responding is a nonselective one. 250 references. (Author abstract modified)

002449 Gay, Patricia E.; Benner, Samuel C.; Leaf, Russell C. Department of Psychiatry, University of Utah Medical Center, 50 N. Medical Drive, Salt Lake City, UT 84132 **Drinking induced by parenteral injections of pilocarpine.** Pharmacology Biochemistry and Behavior. 5(6):633-638, 1976.

To further explore the relationship between parenteral pilocarpine administration and water consumption and to determine if water drinking is related to the cholinomimetic action of the drug, a number of experiments were undertaken with male rats. Parenteral injections of pilocarpine, in doses from 3.75 to 30 mg/kg, reliably produced drinking in water satiated rats. This effect was not diminished by pretreatment with either centrally active (scopolamine, atropine) or peripherally active (methyl scopolamine, methyl atropine) cholinergic blocking agents, suggesting that pilocarpine does not induce drinking via a cholinergic mechanism. Repeated injections of low doses, but not high doses, of pilocarpine augmented drinking over trials. 8 references. (Author abstract modified)

002450 Gentry, R. Thomas; Wade, George N.; Roy, Edward J. Dept. of Psychology, University of Massachusetts, Amherst, MA 01002 **Individual differences in estradiol-induced behaviors and in neural 3H-estradiol uptake in rats.** Physiology & Behavior. 17(2):195-200, 1976.

The effects of estradiol benzoate (EB) treatment on food intake, running wheel activity, and sexual receptivity were measured in a group of 14 ovariectomized rats. Rats were then injected with 3H-estradiol-17 beta, and uptake of radioactivity was determined in whole homogenates and cell nuclear fractions of cerebral cortex, preoptic area, hypothalamus, and pituitary gland. During EB treatment the heaviest rats tended to show the greatest anorexia and weight loss, consistent with the hypothesized weight regulating actions of estradiol. In contrast, the activity increases and weight losses induced by EB were unrelated. The three behavioral responses to EB (anorexia, increased activity, and estrus behavior) were completely independent of one another, suggesting that estradiol acts on separate neural substrates to alter these three behaviors. Large amounts of radioactivity were taken up by cell nuclei, with pituitary uptake highest, followed by preoptic area and hypothalamus (which did not differ) and cerebral cortex. However, a greater proportion of the total tissue radioactivity was found in cell nuclei in hypothalamus and preoptic area than in pituitary. Finally, none of the behavioral responses to EB displayed a significant correlation with any of the indices of brain or pituitary 3H-estradiol uptake. 32 references. (Author abstract)

002451 Gianutsos, Gerald. University of Rhode Island **Mechanism and characteristics of drug-induced aggression. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-8949 HC$20.00 MF$10.00 186 p.

The pharmacological alteration of drug induced aggression in naive, morphine dependent and chronically haloperidol treated rats was investigated. Naive rats were treated with apomorphine and aggregated in groups of four for aggression. Results of this study demonstrated the requirement of central dopaminergic stimulation for drug induced aggression, and suggested that the aggression was antagonized by the activity of acetylcholine and serotonin and possibly facilitated by norepinephrine. In addition, it suggested that morphine and haloperidol produce an antiaggression action by different mechanisms, possibly involving a cholinergic component in the case of haloperidol. Finally, the research provided evidence that the dopaminergic supersensitivity following chronic treatment with morphine may be qualitatively or quantitatively different from the supersensitivity following chronic treatment with haloperidol, since spontaneous and amphetamine stimulated aggression are noted only in the former case. It was proposed that morphine interferes with cholinergic and/or serotonergic compensatory mechanisms and that these contribute to the aggression. (Journal abstract modified)

002452 Gibbons, Judith Lynn. Carnegie-Mellon University **Serotonergic mechanisms and predatory aggression: the effects produced by PCPA, tryptophan injections, and a tryptophan-free diet on mouse killing behavior by rats. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-23476 HC$15.00 MF$8.50 226 p.

The role of serotonin (5-hydroxytryptamine, 5-HT) in mousekilling by rats was investigated using para-chlorophenylalanine (PCPA) injections and maintenace on a tryptophan free diet to deplete brain 5-HT and using l-tryptophan injections to increase brain 5-HT. PCPA induced killing in 33% of nonkillers at high doses, while at lower doses killing was facilitated in killers in two different paradigms. Facilitation of the predatory aggression by PCPA was reversed by injections of 5-hydroxytryptophan, the immediate precursor of serotonin. At a dose which facilitated mousekilling, PCPA did not alter the topography of the killing response or induce rat pup killing or general irritability. Food and water intake and open-field activity were somewhat decreased. Injections of 100mg/kg l-tryptophan, the amino acid precursor of serotonin, lengthened the latencies to attack and kill mice and increased brain 5-HT by 37% and 5-HIAA by 73%. Lower doses were ineffective in blocking killing. The 100mg/kg dose also decreased open-field locomotion. Short-term maintenance on a tryptophan free diet decreased brain 5-HT by 40% and 5-HIAA by 40%, induced killing in 57% of nonkillers, and facilitated killing behavior in natural killers. Mousekilling induced or facilitated by the diet was similar in topography to the natural killing response. Results were generally consistent with the hypothesis that brain serotonergic systems have an inhibitory effect on mousekilling by rats. (Journal abstract modified)

002453 Gispen, W. H.; Wiegant, V. M.; Bradbury, A. F.; Hulme, E. C.; Smyth, D. G.; Snell, C. R.; de Wied, D. Div. Molec. Neurobiol., R. Magnus Inst. for Pharm., State U. of Utrecht, Padualaan 8, Utrecht, The Netherlands **Induction of excessive grooming in the rat by fragments of lipotropin.** Nature (London). No. 5588:794-795, 1976.

A study was undertaken to investigate the induction of excessive grooming in the rat by various lipotropin fragments in the absence and presence of an opiate antagonist. The present study was aimed at investigating the nature of the peptide/CNS interaction underlying behavioral effects. Since opiate antagonists suppress ACTH and lipotropin induced behavior, the conclusion that the neural substrate for this behavior is sensitive to ACTH fragments, lipotropin fragments, and opiates is attractive. Intraventricular administration

of low doses of morphine also induces excessive grooming to the same extent as lipotropin. 26 references.

002454 Giurgea, Corneliu. no address **Piracetam: nootropic pharmacology of neurointegrative activity.** In: Essman, W., Current developments in psychopharmacology. New York, Spectrum, 1976. 393 p. v. 3 (p. 223-273).

Physiological mechanisms involved in integrative activity of the brain are reviewed, with emphasis on the telencephalic contribution in higher mammals. Studies on the effects of piracetam in animals and humans which indicate that the drug may directly and preferentially enhance the efficiency of telencephalic integrative activities are reviewed. It has been found that piracetam: 1) protects against hypoxia induced and barbiturate intoxication induced aggressions; 2) facilitates learning and memory in normal and deficient (aged, hypoxic, alcoholic, sensory deprived) animals in a variety of experimental models; 3) facilitates interhemispheric transfer of information through callosal transmission, as demonstrated by recording of evoked potentials and behavioral studies; and 4) produces these CNS effects without having sedative, analeptic, or autonomic effects. Possible therapeutic applications for piracetam are suggested. It is also suggested that piracetam is the first of a new class of CNS active drugs, the nootropics, i.e. drugs that directly affect the higher integrative mechanisms of the brain. 152 references.

002455 Gold, Paul E.; Van Buskirk, Roderick. Department of Psychobiology, School of Biological Sciences, University of California, Irvine, CA 92717 **Effects of posttrial hormone injections on memory processes.** Hormones and Behavior. 7(4):509-517, 1976.

The effect on memory of posttrial subcutaneous injections of epinephrine (EPI), norepinephrine (NE), adrenocorticotropic hormone (ACTH), growth hormone (GH) vasopressin or corticosterone were examined in rats trained in a passive avoidance task. Animals which received ACTH, EPI or NE had significantly better retention performance 24 hr after training than did saline controls. Large doses of ACTH impaired retention performance. ACTH and NE injections administered 2 hr after training had no significant effect on retention. Immediate postrial injections of vasopressin, GH or corticosterone did not significantly enhance retention. It is concluded that EPI, NE and ACTH can enhance memory processes if injected shortly after training. The results are consistent with the view that hormonal consequences of an experience, particularly EPI, NE or ACTH release, may normally have a modulatory influence on memory processes in untreated animals. It is suggested that other posttrial treatments which enhance or impair later retention performance may act through hormonal mechanisms. 25 references. (Author abstract modified)

002456 Goldberg, Steven R. New England Regional Primate Research Center, One Pine Hill Drive, Southborough, MA 01772 **Conditioned behavioral and physiological changes associated with injections of a narcotic antagonist in morphine-dependent monkeys.** Pavlovian Journal of Biological Studies. 11(4):203-221, 1976.

A series of experimental studies with rhesus monkeys illustrating ways in which behavior of morphine dependent subjects can be modified and controlled by environmental stimuli associated with injections of narcotic antagonists was reviewed. In the first experimental report it was found that environmental stimuli which are repeatedly associated with the nalorphine induced withdrawal syndrome in morphine dependent monkeys acquire the ability to produce a variety of conditioned behavioral and physiological responses. Morphine dependent rhesus monkeys were studied under a fixed-ratio schedule where every tenth lever press produced a food pellet. After several pairings of a stimulus (light or tone) with intravenous injection of a dose of nalorphine which produced an immediate and severe withdrawal syndrome, onset of the stimulus alone produced conditioned suppression of lever pressing, heartrate decrease, vomiting, and salivation. Conditioned suppression of responding and conditioned heartrate changes persisted in postdependent monkeys for 1 to 4 months after termination of chronic morphine treatment. No conditioned electrocardiogram, respiration or temperature changes were ever seen. A second group of morphine dependent rhesus monkeys was studied under a schedule where every lever press produced an intravenous injection of morphine. After 10 pairings of a light with the intravenous injection of a dose of nalorphine which produced marked withdrawal signs and increased responding for morphine, presentation of the light and injection of saline produced conditioned increases in responding for morphine. A third group of morphine dependent rhesus monkeys was studied under a schedule where every nth lever press (n-1 to 10) terminated a stimulus light associated with periodic injections of nalorphine or naloxone; lever press responding was engendered and subsequently maintained. Thus, stimuli associated with the nalorphine induced or naloxone induced withdrawal syndrome can either suppress, enhance or maintain behavior depending on the schedule conditions. 37 references. (Author abstract modified)

002457 Goldberg, Steven R.; Gonzalez, Fernando A. New England Regional Primate Research Center, One Pine Hill Drive, Southborough, MA 01772 **Effects of propranolol on behavior maintained under fixed-ratio schedules of cocaine injection or food presentation in squirrel monkeys.** Journal of Pharmacology and Experimental Therapeutics. 198(3):626-634, 1976.

The effects of propranolol induced alterations in hemodynamic mechanisms on behavior maintained under fixed-ratio schedules of intravenous cocaine injection or food presentation were investigated in squirrel monkeys. Propranolol had no effect on food maintained responding but decreased cocaine maintained responding by approximately 30%. Decreases in cocaine maintained responding after propranolol became increasingly pronounced as the session progressed. Similar progressive decreases in cocaine maintained responding were produced by increasing the dose of cocaine per injection. The results are consistent with the findings of previous studies which indicate that steady state plasma levels of drugs can be increased by propranolol through hemodynamic mechanisms. 30 references. (Author abstract modified)

002458 Graeff, F. G. Department of Pharmacology, Faculty of Medicine, Caixa Postal 301, 14.100 Ribeirao Preto, Sao Paulo, Brazil **Effect of cyproheptadine and combinations of cyproheptadine and amphetamine on intermittently reinforced lever-pressing in rats.** Psychopharmacology (Berlin). 50(1):65-71, 1976.

Effects of the tryptamine antagonist, cyproheptadine, as well as of amphetamine, chlordiazepoxide, and combinations of cyproheptadine with amphetamine on lever pressing behavior of rats were determined. A multiple, fixed-interval, 2 min fixed-ratio, 15 response schedule of water presentation was used. The three drugs affected fixed-interval fixed-ratio responding in a rate dependent way, lower rates being more increased, whereas higher rates were relatively more

decreased. Cyproheptadine increased low response rates to a lesser extent than amphetamine, but increased high response rates that were little affected or only decreased by amphetamine. The combination of cyproheptadine and amphetamine increased response rates to a higher extent than either of the drugs alone. In addition, the rate suppressant effects of the highest doses of amphetamine were also enhanced by cyproheptadine. The results show that cyproheptadine can increase nonpunished responding and suggest that cyroheptadine and amphetamine act synergistically, but through different mechanisms, upon multiple fixed-interval fixed-ratio performance. 24 references. (Author abstract)

002459 Gumulka, S. W.; Dinnendahl, V.; Schonhofer, P. S.; Stock, K. Institut fur Pharmakologie, Abteilung II, Medizinische Hochschule Hannover, Karl-Wiechert Allee 9, D-3000 Hannover 61, Germany **Dopaminergic stimulants and cyclic nucleotides in mouse brain.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 295(1):21-26, 1976.

The effects of dopaminergic stimulants on the cyclic guanosine 3',5'-monophosphate (GMP) content in the medial forebrain and the cerebellum were studied in mice pretreated with dopaminergic antagonists, cholinolytics and agents enchancing gamma-aminobutyric acid (GABAergic) transmission. Low doses of butyrophenones (haloperidol and spiroperidol) inhibited the rise in cyclic GMP levels and the stereotyped behavior induced by amphetamine, but were without effect on the same biochemical and behavioral changes elicited by apomorphine. Higher doses effectively blocked the rise in cyclic GMP levels and the stereotyped behavior elicited by both drugs. The findings suggest that low doses of the dopaminergic antagonists may predominantly act by interfering with the release of dopamine from presynaptic stores, while high doses may act by blockade of the postsynaptic dopaminergic receptor. The rise in cerebellar cyclic GMP levels elicited by dopaminergic stimulants appears not to involve cholinergic transmission, since atropine did not block the effects of the dopaminergic stimulants. Enhancement of GABAergic transmission by diazepam or aminooxyacetic acid antagonized the rise in cerebellar cyclic GMP content induced by the dopaminergic stimulants, but was without effect on the cyclic GMP content in the medial forebrain. Cyclic AMP levels were not affected by any of the drugs in both parts of the brain. 23 references. (Author abstract)

002460 Hata, Taeko; Kita, Tomitaro; Yoneda, Ryozo. Department of Pharmacology, Faculty of Pharmacy, Kinki University, Higashiosaka 577, Japan **Comparison between analgesic activities in SART-stress mice and in normal mice.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):44P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan in March 1976, a comparative study of the analgesic effects of neurotropin (NSP) and other agents in SART stressed (specific stress caused by alternating rhythm in temperature) mice and normal mice was reported. NSP given alone to normal mice resulted in slight analgesic effects as observed with the application of the acetic acid, phenylquinone writhing method, or the modified Randall-Selitto method. Very little effect was seen when the D'Armour-Smith method was used. Synergism was evident when NSP and aminopyrine or NSP and morphine were given concomitantly and the acetic acid or phenylquinone writhing methods were applied. The analgesic effects of morphine, levomepromazine, imidazole acetic acid and particularly NSP were greater in SART stress mice than in normal mice except with the D'Amour-Smith method when only NSP had a greater effect in SART stress mice than in normal mice. (Author abstract modified)

002461 Heal, D. J.; Green, A. R.; Boullin, D. J.; Grahame-Smith, D. G. MRC Unit and University Department of Clinical Pharmacology, Radcliffe Infirmary, Oxford OX2 6HE, England **Single and repeated administration of neuroleptic drugs to rats: effects on striatal dopamine-sensitive adenylate cyclase and locomotor activity produced by tranylcypromine and L-tryptophan or L-dopa.** Psychopharmacology (Berlin). 49(3):287-300, 1976.

The behavioral model described by Grahame-Smith (injection of tranylcypromine followed by L-tryptophan measurement of the hyperactivity that results from the increased synthesis of 5-hydroxytryptamine (5-HT) and its probable release onto receptors to produce functional activity was used to determine the 5-HT response in rats to neuroleptic drugs. The hyperactivity which follows injection of tranylcypromine and L-dopa and which appears to be the result of stimulation of dopaminergic systems in the brain was used to measure the dopamine response. Using chlorpromazine, an investigation was made into whether the inhibition of the dopamine induced locomotor activity was accompanied by inhibition of dopamine sensitive adenylate cyclase in vivo as is demonstrated in vitro. Rats treated for 4 or more days with chlorpromazine alpha-flupenthixol, spiroperidol and haloperidol subsequently showed enhanced locomotor activity in response to tranylcypromine and L-dopa. Administration of those drugs which did not block hyperactivity acutely did not result in enhancement. Only chlorpromazine, when given for 4 days, enhanced the hyperactivity response following tranylcypromine and L-tryptophan, probably because the drug also blocks 5-HT receptors. In rats displaying enhanced sensitivity of striatal adenylate cylase to dopamine. 54 references. (Author abstract modified)

002462 Heise, George A.; Conner, Robert; Martin, Richard A. Department of Psychology, Indiana University, Bloomington, IN 47401 **Effects of scopolamine on variable intertrial interval spatial alternation and memory in the rat.** Psychopharmacology (Berlin). 49(2):131-137, 1976.

A repeated measures procedure, variable intertrial interval (ITI) spatial alternation, was used to assess scopolamine effects on memory, and to compare effects of the drug on discrimination processes with effects on storage. Rats learned in two stages to press left levers and right levers in alternation on discrete trials separated by 5 different ITI's presented in random order. Alternation response occurrence declined moderately but significantly with increasing ITI duration in both the alternating discrimination and variable ITI spatial alternation stages; response occurrence was also significantly decreased by scopolamine treatment in both stages. Accuracy of alternating discrimination performance was not significantly altered by either ITI duration or scopolamine treatment. Accuracy of variable ITI spatial alternation performance on a trial varied inversely with the duration of the ITI that preceded the trial. Scopolamine significantly reduced accuracy of lever pressing in variable ITI spatial alternation but did not alter the slope of the curves relating accuracy to ITI duration. These effects indicate that scopolamine impairs discrimination processes but does not alter memory storage. 15 references. (Author abstract modified)

002463 Herman, Z. S.; Brus, R.; Drybanski, A.; Szkilnik, R.; Slominska-Zurek, J. Department of Pharmacology, Marksa 38, 41-808 Zabrze, Poland **Influence of 6-hydroxydopamine on the behavioral effects induced by apomorphine or clonidine in rats.** Psychopharmacology (Berlin). 50(1):73-80, 1976.

The behavioral effects of apomorphine (AP) and clonidine (CL) in the central nervous system were studied in rats treated

with 6-hydroxydopamine (6-OHDA). The time of duration of several components of behavior and the degree of irritability of rats were measured. Moreover, open-field and hole test were performed. The lower dose of AP did not affect behavior of rats. The higher dose increased the locomotor and exploratory activity of animals. 6-OHDA potentiated the effects of AP. CL had a depressive effect on the rats' behavior, which was potentiated by 6-OHDA. Although a high dose of CL had no effect on behavior, lower doses were excitatory. This type of behavior was abolished by 6-OHDA. In conclusion, central chemical sympathectomy caused increased senstitivity of the central nervous system on AP. Excitatory behavioral effects of CL in low dosage may be connected with stimulation of central adrenergic receptors. Depressive behavioral effect of CL in high dosage is unspecific. Central chemical sympathectomy affects the reactivity of dopaminergic and noradrenergic neurons by different methods. 43 references. (Author abstract)

002464 Hoffmeister, F. Institut fur Pharmakologie der Bayer AG, D-5600 Wuppertal 1, Germany **Emotional and motivational aspects of drug taking behavior of animals.** In: Airaksinen, M., CNS and behavioural pharmacology. Elmsford, New York, Pergamon Press, 1976. 344 p. v. 3. (p. 185-196).

In a paper presented at the Sixth International Congress of Pharmacology held in Helsinki, Finland in July, 1975, a series of studies of the ability of several drugs to motivate self-administration by rhesus monkeys (positive reinforcement) or to motivate avoidance of administration by monkeys (negative reinforcement) is reported. Monkeys were trained to self-administer infusions of codeine. After responding was established, different doses of heroin, codeine, pentobarbital, dextroamphetamine, nalorphine, cyclazocine, chlorpromazine, and imipramine were substituted for the initial codeine dose. Heroin, codeine, pentobarbital, and dextroamphetamine maintained stable self-administration behavior in a dose dependent manner; however, chlorpromazine, imipramine, nalorphine, and cyclazocine did not, indicating that chlorpromazine, imipramine, nalorphine, and cyclazocine do not have the ability to motivate an animal for self-injection. In a second group of experiments, monkeys were trained to press a lever to turn off a white light which was associated with a noxious electric stimulus, in order to prevent (avoidance) or terminate (escape) the shock. The electric shock was then replaced by infusions of imipramine, pentobarbital, dextroamphetamine, codeine, or heroin, which were all accepted by the animals. However, when the shocks were replaced by infusions of nalorphine or cyclazocine, avoidance/escape behavior was initiated and maintained. Chlorpromazine abolished avoidance/escape behavior during the first 3 days of testing but initiated avoidance/escape behavior during the second 3 day testing period. The results suggest that: 1) heroin, codeine, pentobarbital, and dextroamphetamine are able to motivate monkeys to self-administer them; 2) nalorphine, cyclazocine, and chlorpromazine are able to motivate monkeys to avoid their administration; and 3) imipramine influences neither self-administration nor drug avoidance behavior. The results are discussed in terms of the emotional states which these drugs produce in humans. 14 references.

002465 Holmgren, Bjorn; Urba-Holmgren, Ruth; Valdes, Mitchell. National Center of Scientific Investigations, Apartado 6990, La Habana, Cuba **Spontaneous and amphetamine induced head-shaking in infant rats.** Pharmacology Biochemistry and Behavior. 5(1):23-28, 1976.

Infant rats were injected with 5mg/Kg D-amphetamine, and the amphetamine induced head shaking was compared to spontaneous head shaking of control rats. Head shaking is slightly anticipated and significantly increased in occurrence and duration by the administration of amphetamine, with a maximal effect of the drug on the ninth day after bith. The rate of amphetamine induced rhythmic head oscillations increases with age from below five cycles per second on the fifth day to about nine cycles per second on the tenth day. The results are discussed in relation to maturation of both the underlying catecholaminergic pathways, activated by D-amphetamine, and the stretch reflex systems of the head and neck muscles participating in the rhythmic activity. Emphasis is placed on the difference between head shaking and stereotyped activity. 29 references. (Author abstract modified)

002466 Holtzman, Stephen G.; Shannon, Harlan E.; Schaefer, Gerald J. Dept. of Pharmacology, Emory University, Atlanta, GA 30322 **Discriminative properties of narcotic antagonists.** Psychopharmacology Communications. 2(4):315-318, 1976.

At a symposium on the research aspects of drug induced discrimination stimuli conducted in connection with the annual meeting of the Behavioral Pharmacology Society, Durham, New Hampshire, in May 1976, an investigation of the proposal, that the component of drug action responsible for the subjective effects produced in man by analgesics with mixed narcotic agonist and narcotic antagonist properties is related to the component of action responsible for discriminative effects in animals, was reported. In rats trained to discriminate morphine from saline, four drugs with morphinelike activity (butorphanol, nalmexone, pentazocine, and profadol) could be substituted for the training dose of morphine. Drugs with prominent similarities to cyclazocine activity (cyclazocine, ketocyclazocine, levallorphan, nalorphine, nalbuphine, and oxilorphan) failed to substitute for morphine. In squirrel monkeys, the findings with those similar to the cyclazocine drugs correlated with those in the rat; however, some of the morphinelike drugs that substituted for morphine in the rat showed less activity in the monkey. There appears to be a good correspondence between the patterns of discriminative effects of the narcotic antagonists relative to the training drugs in infrahuman species and the subjective effects that these drugs produce in man. It is suggested that drug discrimination paradigms may provide an animal model for the preclinical evaluation of this important component of action of the narcotic antagonists. 6 references. (Author abstract modified)

002467 Horibe, Masahiro; Sorimachi, Masayuki; Hino, Kenji; Shibuya, Takeshi. Department of Pharmacology, Tokyo Medical College, Tokyo, Japan **Behavioral and neuropharmacological investigations concerning one of newer central acting muscle relaxants, chlorphenesin carbamate.** Journal of the Tokyo Medical College (Tokyo). 34(6):1011-1022, 1976.

Behavioral and neuropharmacological experiments were performed on rats, rabbits, and cats with one of the central acting muscle relaxants, chlorphenesin carbamate (CPS). After injection of CPC, postural relaxation of naive behavior in these animals was observed. The condition avoidance response of rats and their lever pressing behavior was depressed at a dose level of 25 to 50mg/kg CPC. CPS also induced slow wave patterns in the neocortical EEG of rabbits at a dose level of 100mg/kg. It was concluded that CPC produces muscle relaxation in various animal species and does not affect the EEG arousal response. 11 references. (Author abstract modified)

002468 Howard, J. L.; Pollard, G. T.; Rohrbach, K. W.; Harto, N. E. Department of Pharmacology, Burroughs Wellcome Co., 3030 Cornwallis Rd., Research Triangle Park, NC

27709 **Effect of beta-phenylethylamine and d-amphetamine on electrical selffstimulation of brain.** Pharmacology Biochemistry and Behavior. 5(6):661-664, 1976.

Since d-amphetamine produces a dose related increase in the rate of bar pressing for electrical stimulation of the medial forebrain bundle, the effect of beta-phenylethylamine on this behavioral paradigm was investigated, in order to further examine the putative similarities of action of these 2 drugs on behavior in rats. Male Long-Evans rats implanted with bipolar electrodes self-administered 250 msec 60 Hz constant current sine wave trains over a 30 -70 microA range of intensities in daily 20 min tests. Over a range of 1 to 40mg/kg of beta-phenylethylamine, a dose related decrease in self-stimulation rate was observed. Pretreatment with para-chlorophenylalanine or alpha-methyl-para-tyrosine did not alter the response to 2.5or 30mg/kg of beta-phenylethylamine. Since within the dose range of beta-phenylethylamine used in this study a dose related increase in locomotor activity was observed and since d-amphetamine increases self-stimulation rate at doses that increase locomotor activity, it would seem that there are qualitative differences in the actions of d-amphetamine and beta-phenylethylamine on behavior. 18 references. (Author abstract modified)

002469 Hynes, Martin D.; Gianutsos, Gerald; Lal, Harbans. Dept. of Pharmacology, College of Pharmacy, Univ. of Rhode Island, Kingston, RI 02881 **Effects of cholinergic agonists and antagonists on morphine-withdrawal syndrome.** Psychopharmacology (Berlin). 49(2):191-195, 1976.

The effects of pilocarpine, atropine, and dexetimide on the occurrence and intensity of morphine withdrawal symptoms were studied in rats. Pilocarpine reduced body shakes and aggression, but increased diarrhea and weight loss. Pretreatment with atropine blocked all of the effects of pilocarpine on withdrawal symptoms. Methylscopolamine pretreatment blocked only the effect on diarrhea. Administration of atropine or dexetimide produced no significant effect on any of the withdrawal signs. A role for a central cholinergic mechanism in narcotic withdrawal is suggested. 24 references. (Author abstract modified)

002470 Ichimura, Masamichi; Muroi, Kimiyo; Mega, Ayako. Life Sciences Laboratory, Ajinomoto Co., Inc., Yokohama 244, Japan **Effects of L-5-hydroxytryptophan on biting behavior induced by long-term isolation in mice.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):39P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study of the effects of L-5-hydroxytryptophan (L-5-HTP) on biting behavior induced by long-term isolation in mice was reported. L-5-HTP caused a dose dependent inhibition of biting behavior in isolated mice. An aromatic amino acid decarboxylase inhibitor, Ro 4-4602, caused biphasic actions on the inhibitory effect of L-5-HTP; lower doses of Ro 4-4602 potentiated the inhibitory effect of L-5-HTP, but higher doses of Ro 4-4602 antagonized the effect of L-5-HTP. In both cases, Ro 4-4602 inhibited diarrhea, which was observed as an index of a peripheral action of L-5-HTP. Apparent relationships were observed between the inhibitory effect of L-5-HTP on biting behavior and concentrations of brain 5-HT. L-5-Hydroxytryptophan ethyl ester as well as L-5-HTP caused an inhibitory effect on biting behavior. D-5-Hydroxytryptophan and L-tryptophan showed no effect on biting behavior. L-DOPA showed an accelerative tendency toward biting behavior. It is concluded that the inhibitory action of L-5-HTP on biting behavior in isolated mice is a central action, and seems to be dependent on an increase in concentrations of brain 5-HT. The therapeutic effect of L-5-HTP on biting in the Lesch-Nyhan syndrome may be explained by a similar mechanism. (Author abstract modified)

002471 Imamura, Goro. Tokyo University, Tokyo, Japan **The effect of amytal on smell discrimination learning in albino rats.** Annual of Animal Psychology (Tokyo). 26(1):50, 1976.

In a summary of a paper read to the 36th Symposium of Japanese Animal Psychologists held in June 1976 at Osaka University, experimental results on the effects of amytal on smell discrimination in male rats is reported. In the first experiment, amytal in 15mg/kg doses did not affect performance. In a second experiment 20 to 25mg/kg was administered in a discrimination test between two different smelling objects. In the first part of the training, amytal was administered and in the second part a saline solution was administered. Results indicated a 50% increase in successful discrimination in the latter part of the experiment.

002472 Irizawa, Naoki; Iwahara, Shinkuro; Fukuda, Yukio. Tokyo University of Education, Tokyo, Japan **The effect of inner septum damage (rats) on drug-dependent discriminative learning.** Annual of Animal Psychology (Tokyo). 26(1):56, 1976.

In a paper read to the 36th Symposium of Japanese Animal Psychologists held in June 1976 at Osaka University, an experiment in which pentobarbital was administered (10mg/kg) to male Wistar-Imamich rats to induce drug condition dependence learning (SDL) and hippocampus theta-rhythm changes is reported. Water and food intake, and electrical shock avoidance discrimination behavior was monitored in the rats. Due to inner septum damage, loss of theta-waves in the experimental group was possible, just as it was for the control group, and SDL could be induced. Results of the experiment did not support Sach's opinion that the hippocampal function is related to SDL.

002473 Ishikawa, Koichi; Saito, Shoji. Department of Pharmacology, School of Medicine, Nihon University, Tokyo 173, Japan **Effects of various drugs on learning behavior of animals: V. Effects of picrotoxin and amino-oxy acetic acid.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):41P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study of the effects of picrotoxin (PTX) and amino-oxyacetic acid (AOAA) on discrimination learning behavior in rats was reported. Rats were trained to perform light and dark discrimination learning reinforced by water for 1 hr per day. Each animal was injected with PTX or AOAA immediately or 60 min after training. In dose levels of 2mg/kg or more, PTX, a selective antagonist of gamma-aminobutyric acid (GABA), impaired learning when the drug was injected immediately after training. When injected immediately after training, 25mg/kg or more of AOAA improved learning. Neither PTX nor AOAA affected learning when the drugs were injected 60 min later. It is suggested that the GABAergic system may play an essential function in memory formation, and that the formation could require a certain time course. (Author abstract modified)

002474 Iwasaki, Morio; Kobayashi, Masafumi; Sato, Mikio. Department of Pharmacology, Nihon University School of Dentistry, Tokyo 101, Japan **Role of brain serotonin on "methamphetamine-induced stereotypy" in sham-operated or adrenalectomized rats -- effects of alpha-MMT, p-CPA or L-DOPA, in particular --** . Japanese Journal of Pharmacology (Kyoto). 26(Supplement):35P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study of the role of brain serotonin (5-HT, 5-hydroxytryptamine) on methamphetamine induced stereotypy in sham operated and adrenalectomized rats was reported. Norepinephrine (NE) and 5-HT contents in the brain were decreased by methamphetamine, and enhanced by the action of a monoamine oxidase inhibitor (MAOI). Decreases in brain NE occurred after pretreatment with DL-alpha-metyl-m-tyrosine (MMT), and 5-HT depletion occurred with p-chlorophenylalanine (p-CPA). Some pattern of methamphetamine stereotypies was delayed with p-CPA, but not with the other above mentioned drugs. The stereotypy and rate of increase in brain 5-HT after MAOI or methamphetamine plus MAOI were suppressed after adrenalectomy. These results suggest that brain 5-HT may play a role in methamphetamine stereotypy and that the effect of methamphetamine on the rat brain decreases after adrenalectomy. (Author abstract modified)

002475 Iwasaki, Tsuneo. Institute of Psychology, Tsukuba, University Sakura-mura, Niihari-gun, Ibaraki-ken, 300-31, Japan **Deficient go/no-go discrimination learning in rats under the treatment of chlordiazepoxide.** Japanese Psychological Research (Toyko) 18(3):113-117, 1976.

The effect of chlordiazepoxide (CDP) at a intraperitoneal dose of 20mg/kg upon a go/no-go successive discrimination learning was investigated in the rat to determine if CDP exerts a disruptive effect on the response/suppression process. The subjects were 13 albino rats who had been preliminarily trained enough to travel the runway at their full speed before the go/no-go task was introduced. They were then required to maintain the approach response on the go trials and to suppress it on the no-go trials. The results suggest that the response/suppressing processes do not efficiently function under the treatment of CDP. Daily treatments of CDP significantly retarded the acquisition of the learning, especially the development of the response/suppression on the no-go trials. The present results do not support a possible inhibitory action of CDP on general arousal and/or sensory processes, nor can they be accounted for in terms of the drug's deteriorating effect on peripheral motor systems since little or no increase in the response time on the go trials was observed. Instead, it is concluded that the present results support the hypothesis that CDP might produce a "functional hippocampectomy" based on the finding that the animals under this drug show deficits in various behavioral paradigms such as two-way avoidance, spontaneous alternation, reversal learning and successive brightness discrimination. It suggests that the acquisition of a go/no-go type successive discrimination is mediated by the central inhibitory mechanisms, which are susceptible to hippocampectomy and treatment of CDP. Further studies are needed to clarify whether CDP exerts it behavioral effect by depressing the hippocampal function directly or indirectly. 11 references.

002476 Iwazaki, Yasuo; Fukuda, Yoshio; Suzuki, Shizuya. no address **The effect of chlordiazepoxide on go/no-go learning related to hunger activity in rats.** Annual of Animal Psychology (Tokyo). 26(1):49-50, 1976

In a paper read to the 36th Symposium of Japanese Animal Psychologists held in June 1976 at Osaka University, the control release function of chlordiazepoxide (CDP) was investigated in a go/no go type of successive discrimination learning experiment with rats trained by light stimulus. One group was given daily doses of 20mg/kg of CDP and the control group was given a saline solution. The results indicated that the CDP group required significantly more trials to attain a prescribed level of performance. Also, CDP delayed the running about reaction observed in the control group rats in the no go trial. It was concluded that CDP has a functional control over reactions (a blocking effect), thus supporting the control release theory.

002477 Izquierdo, Ivan. Departamento de Fisiologia, Escola Paulista de Medicina, Rua Botucatu 882, 04023 Sao Paulo, SP, Brazil **A pharmacological separation of buzzer-shock pairing and of the shuttle-shock contingency as factors in the elicitation of shuttle responses to a buzzer in rats.** Behavioral Biology. 18(1):75-87, 1976.

The effect of tyramine, LSD, LSD + dibenamine and diazepam was tested in the rat on two experimental paradigms: one in which buzzers and shocks were "paired" but in which shocks were given on all trials independently of responses and another one in which the buzzer shock interval was varied at random but shocks were contingent upon shuttling to the buzzer. In the former test, LSD and diazepam increased shuttling to the buzzer, whereas tyramine and dibenamine had no effect and dibenamine partially blocked the action of LSD. In the latter test, tyramine and LSD + dibenamine depressed responding, diazepam increased it, and LSD and dibenamine on their own had no effect. These drugs may affect two-way avoidance possibly by an action on the "contingency" mechanism. Present data also suggest that drive and what is called pairing and contingency are separable factors. 21 references. (Author abstract modified)

002478 Izquierdo, Ivan; Cavalheiro, Esper A. Departamento de Fisiologia, Escola Paulista de Medicina, Rua Botucatu 862, 04023 Sao Paulo, SP, Brazil **Three main factors in rat shuttle behavior: their pharmacology and sequential entry. in operation during a two-way avoidance session.** Psychopharmacology (Berlin). 49(2):145-157, 1976.

The effects of eserine, nicotine, atropine, methylatropine, clonidine, phenoxybenzamine, apomorphine and haloperidol on shuttle responses to a buzzer (SB) were studied in rats using four behavioral paradigms designed to determine the sequence in which drive (D), pairing (P), and contingency (C) may enter in operation as factors in shuttle behavior. SB performance in sessions consisting of 10 successive blocks of 5 buzzers was interpreted as showing that during the first 10 buzzers, D was the main factor influencing SB performance; after the third block of 5 buzzers, C became a factor, and P assumed some control over SB behavior only from the fifth block on. Eserine depressed SBs in the paradigm in which only D was a factor; its effect was antagonized by atropine and methylatropine. Clonidine depressed responding in paradigms in which P was a factor; its effect was blocked by phenoxybenzamine. Nicotine, eserine and apomorphine increased SB performance, while atropine, methylatropine and haloperidol decreased SB performance in the paradigms in which C was a factor. Nicotine and eserine could be antagonized by either atropine or methylatropine, while apomorphine was antagonized by haloperidol. The possibilities are discussed of the existence of: 1) a peripheral cholinergic mechanism which inhibits drive; 2) a similar mechanism which favors operation of the contingency factor; 3) a dopaminergic mechanism in contingency; and 4) a central adrenergic inhibitory mechanism in pairing. 28 references.

002479 Kaesermann, H. P.; Peters, G. Institut de Pharmacologie, Universite de Lausanne, Rue du Bugnon 21, CH-1011 Lausanne, Switzerland **Dipsogenic effects of intracranial**

renin, the angiotensins and their tetradecapeptide precursor in the rat. Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 294(Supplement):R17, 1976.

In a paper presented at a pharmacology meeting in Hannover, Germany, on September 14-17, 1976, the dipsogenic effects of intracranial renin, the angiotensins, and tetradecapeptide in mice were discussed. Within 20 hours after lateral preoptical injections, food intake was slightly increased by tetradecapeptide and decreased by tepromide plus renin. It is concluded that the dipsogenic effect of tetradecapeptide does not appear to depend on transformation into angiotensins. (Author abstract modified)

002480 Kastin, Abba J.; Scollan, Elizabeth L.; King, Maurice G.; Schally, Andrew V.; Coy, David H. Veterans Administration Hospital, 1601 Perdido Street, New Orleans, LA 70146 **Enkephalin and a potent analog facilitate maze performance after intraperitoneal administration in rats.** Pharmacology Biochemistry and Behavior. 5(6):691-695, 1976.

To examine the behavioral actions of systemic administration of enkephalin in a learning situation, met-enkephalin and its analog (D-Ala2)-met-enkephalin-NH2 were administered intraperitoneally at a dose of 80 microgram/kg body weight to hungry rats which were tested over 3 days for their ability to run a complex, 12 choice Warden maze for a reward of food. Animals receiving either peptide negotiated the maze significantly faster (74.1and 73.5vs 128.8sec) and made significantly fewer errors (5.5and 5.4vs 9.1) than animals receiving the diluent vehicle. These findings did not seem to be explained by differences in appetite, thirst, olfaction, or general activity. Rats injected in a preliminary study with an analog, (D-Phe4)-met-enkephalin, which has essentially no opiate activity appeared to run the maze as fast as rats injected with (D-Ala2)-met-enkephalin-NH2 and with just as few errors. Injection of morphine seemed to result in slower running times and more errors in the maze. These results demonstrate that enkephalin and some of its analogs can exert significant behavioral changes after intraperitoneal administration and that these behavioral effects probably can be dissociated from the opiate effects. 15 references. (Author abstract)

002481 Katz, Jonathan; Catravas, George N. Department of Neurobiology, Armed Forces Radiobiology Research Institute, Bethesda, MD 20014 **Cerebellar cGMP levels reduced by morphine and pentobarbital on a dose- and time-dependent basis.** Biochemical Pharmacology (Oxford). 25(22):2543-2546, 1976.

The effects of morphine and pentobarbital on cyclic GMP (cGMP) levels in rat cerebellum, demonstrating a dramatic depression of cGMP by morphine and confirming and extending related work on pentobarbital effects on cerebellar cGMP levels is presented. Using a noxious heat stimulus, rats chronically treated with morphine were defined as tolerant when they responded as quickly as controls to the stimulus. Rats acutely treated with morphine responded much more slowly to the stimulus, and as tolerance to morphine was acquired over the 10 day schedule, response time decreased until it equaled that of the controls. It is concluded that morphine and pentobarbital reduce cerebellar cGMP upon acute administration, as well as induce ataxia/catatonia. 25 references.

002482 Kelleher, R. T.; Morse, W. H. New England Regional Primate Research Center, Southborough, MA 01772 **Effects of drugs on behavior controlled by noxious stimuli.** In: Airaksine, M., CNS and behavioural pharmacology. Elmsford, New York, Pergamon Press, 1976. 344 p. v. 3. (p. 175-184).

In a paper presented at the Sixth International Congress of Pharmacology held in Helsinki, Finland in July, 1975, studies of patterns of behavior controlled by different schedules of delivery of electric shock are reviewed with emphasis on scheduled controlled behavior as a concept of critical importance in understanding the behavioral effects of drugs. Studies reviewed include those in which the effects of chlorpromazine and/or dextroamphetamine on responding were examined in monkeys under different schedules of: 1) termination of noxious stimulus (electric shock), i.e.,escape; 2) termination of stimuli associated with electric shock; and 3) presentation of electric shock. Other studies include those of the effects of chlordiazepoxide and meprobamate on behavior maintained by noxious stimuli and studies in rats of the effects of various drugs on behavior suppressed by noxious stimuli (punished responding). The data indicate that the patterns of behavior controlled by a noxious stimulus depend upon how it is scheduled and that the effects of drugs depend upon the schedule controlled pattern of responding. Chlorpromazine decreases rates of responding under various schedules in which electric shocks are used. Chlordiazepoxide or meptrobamate markedly increase rates of responding whether maintained by electric shock or suppressed by electric shock, suggesting that minor tranquilizers have a general tendency to increase low rates of responding. Dextroamphetamine increases rates of responding, especially rates that are initially low, even when responding is maintained by schedules of response dependent electric shock, but tends to decrease rates of responding that are suppressed by response dependent electric shock. It is concluded that the behavioral effects of drugs depend not on the noxious stimuli as such but rather on how they control behavior. 22 references.

002483 Kelly, P. H.; Moore, K. E. Department of Pharmacology, Michigan State University, East Lansing, MI 48824 **Mesolimbic dopaminergic neurones in the rotational model of nigrostriatal function.** Nature (London). No. 5579:695-696, 1976.

To determine whether mesolimbic dopaminergic neurones are involved in drug induced rotational behavior in rats with unilateral lesions of the nigrostriatal pathway, adult male rats were intrastriatally injected with 6-hydroxydopamine (6-OHDA) into the right caudate nucleus and bilaterally injected with 6-OHDA into the nucleus accumbens and rotational behavior induced by injections of amphetamine sulphate or apomorphine was measured. Sixty days later the rats were sacrificed and assessed for regional catecholamine content. Dopamine concentrations in the right striata, nucleus accumbens and olfactory tubercle were found to be reduced, neocortical noradrenaline content was also reduced. Results indicate that acitivity in the mesolimbic dopaminergic system is as important as an imbalance of striatal dopaminergic activity for the expression of drug induced rotational behavior. The implication of these findings for the use of rotational models in assessing the effects of drugs as agonists or antagonists at dopamine receptors are discussed. It is concluded that a drug induced behavioral expression of nigrostriatal output, rotation, is markedly modified by the activity at mesolimbic dopamine receptors. Therefore activity at mesolimbic dopamine receptors may also modify nigrostriatal activity in the undrugged animal and the mesolimbic and nigrostriatal systems may interact physiologically in the control of motor behavior. 27 references.

002484 Kleinrok, Z.; Poddubiuk, Z. **M. Department of Pharmacology, Institute of Clinical Pathology, Medical School, Jac-**

zewskiego 8, 20-090 Lublin, Poland **A comparison of the central action of some prostaglandins /PGs/ in rats.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 294(Supplement):R14, 1976.

In a paper presented at a pharmacology meeting in Hannover, Germany, September 14-17, 1976, a report is made of experiments carried out on Wistar rats, in which the central depressant action of prostaglandins (PGs) given into lateral brain ventricle was shown. This action was observed in the following tests: body temperature, locomotor activity, amphetamine induced hyperactivity, open-field behavior, anesthesia induced by various narcotics, and rota rod. The depressant action markedly differed between various PGs both as to potency and duration. All PGs studied increased free acetylcholine (ACh) concentrations whereas total ACh concentration was enhanced only by PGs of F series. It is concluded that the investigations suggest that PGs tested exert both direct and indirect action on the central nervous system of rats. (Author abstract modified)

002485 Koranyi, L; Tamasy, V.; Lissak, K.; Kiraly, I.; Borsy, J. Institute of Physiology, University Medical School, H-7643 Pecs, Hungary **Effect of thyrotropin-releasing hormone (TRH) and antidepressant agents on brain stem and hypothalamic multiple unit activity in the cat.** Psychopharmacology (Berlin). 49(2):197-200, 1976.

The effects of thyrotropin releasing hormone (TRH), desipramine and imipramine on the electroencephalogram (EEG) and multiple unit activity (MUA) in the mesencephalic reticular formation (MRF), area hypothalami posterior (PH), and area hypothalami anterior (AH) were studied in chronically implanted freely moving cats. Desipramine and imipramine produced a dose dependent decline of MUA in all structures with the most significant decrease occurring in the PH. Single injections of TRH produced gross behavioral changes characterized by intermittent somatic symptoms and vegetative symptoms including vomiting, miosis, hyperventilation, urination, and defecation with variable changes in MUA. Repetitive TRH treatment resulted in failure of the gross behavioral changes to develop and changes in MUA similar to those induced by single injections of desipramine and imipramine. In contrast to desipramine and imipramine, TRH did not suppress paradoxical sleep cycles. 28 references. (Author abstract modified)

002486 Kostowski, W.; Czlonkowski, A.; Rewerski, W.; Piechocki, T. Dept. of Pharmacology, Inst. of Physiological Sciences, Krakowskie Przedmiescie 26/28, 00-927 Warszawa, Poland **Aggressivity, isolation and analgesic action of morphine in rats and mice** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 294(Supplement):R17, 1976.

In a paper presented at a pharmacology meeting in Hannover, Germany, on September 14-17, 1976, a determination of analgesic effects of morphine in grouped and isolated rats and mice was reported. Isolated animals developed altered behavioral patterns including mouse killing attitude in some rats and mutual aggressiveness in mice. Analgesic effects of morphine were assessed with the tail compression or the hot plate method. Isolated rats, both killers and nonkillers, showed decreased response to morphine. Both aggressive and nonaggressive isolated mice showed increased response to morphine. (Author abstract modified)

002487 Kovacs, Gabor L.; Telegdy, Gyula. Department of Pathophysiology, University Medical School, Szeged, Hungary **Inhibitory effect of midbrain raphe stimulation on the maintenance of an active avoidance reflex.** Pharmacology Biochemistry and Behavior. 5(6):709-711, 1976.

To elucidate the effect of midbrain raphe stimulation on the maintenance of a previously trained active avoidance reflex and its biochemical correlates, performance of an active avoidance "bench jumping" reflex was studied in rats during stimulation of the midbrain raphe nuclei. Raphe stimulation (10 cps 0.2msec, 2.5to 5.0V) inhibited the performance of the reflex. A serotonin receptor blocker (methysergide, 2.0mg/kg intraperitoneally) increased the reflex performance in nonstimulated animals and prevented the action of raphe stimulation. The data indicate that the cerebral serotoningergic system might have an inhibitory control over the performance of conditioned avoidance reflex. 30 references. (Author abstract)

002488 Kuribara, Hisashi; Ohashi, Kyoichi; Tadokoro, Sakutaro. Behavior Research Inst., School of Medicine, Gunma Univ., Maebashi 371, Japan **Rat strain differences in the acquisition of conditioned avoidance responses and in the effects of diazepam.** Japanese Journal of Pharmacology (Kyoto). 26(6):725-735, 1976.

Wistar, Sprague-Dawley and Holtzman adult male albino rats were trained to press a lever to avoid electric shocks under Sidman type and discriminated avoidance schedules, and the acquisition processes of avoidance responses and the properties of behavioral baselines were investigated. Under both schedules, Wistar strain rats, though showing poorer results than the other two in the beginning, rapidly progressed with the repetitive training, and finally displayed excellent and stable performances. Sprague-Dawley strain rats were poorer in performances, with delayed acquisition and prolonged warmup effect in the within session performance. The results of Holtzman strain rats ranked between the two. After the establishment of stable behavioral baselines under both schedules, 0.5, 1.0and 2.0mg/kg of diazepam were given subcutaneously, and it was found that in Wistar and Holtzman strain rats, the avoidance responses were inhibited together with increase of delivered shocks in parallel to the doses. In Sprague-Dawley strain rats, however, the avoidance responses were conversely improved with 0.5and 1.0mg/kg, while such tended to be inhibited with 2.0mg/kg, with marked concomitant ataxia. As definite strain differences in avoidance response were demonstrated, selection of the most appropriate strain should be made when designing behavioral experiments. 23 references. (Author abstract modified)

002489 Kuribara, Hisashi; Okuizumi, Kiyoko; Ogawa, Haruyoshi; Tadokoro, Sakutaro. Behavior Research Institute, School of Medicine, Gunma University, Maebashi 371, Japan **Enhancing effects induced by repeated administrations of diazepam on conditioned suppression in rats.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):40P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study of the effects induced by repeated administrations of diazepam on conditioned suppression in rats was reported. Rats were trained to produce three types of the conditioned suppression under fixed ratio (FR 30) schedule of food or water reinforcement with simultaneous delivery of electric shock. When diazepam was given to rats for 10 days, attenuation of the conditioned suppression became progressively prominent up to the 5th day and then the maximum effect was maintained. FR responses decreased for about 3 days and then recovered to the initial levels. A similar attenuating effect to the conditioned suppression was observed by weekly administrations of the same dose. It is suggested that repeated administrations of a drug

are necessary for assay of the antianxiety effect. The method of unavoidable shock in the schedule may play an important role in developing a clear attenuation of the conditioned suppression. (Author abstract modified)

002490 Kuribara, Hisashi; Tadokoro, Sakutaro. Behavior Research Institute, School of Medicine, Gunma Univ., Maebashi 371, Japan **Cumulative effects of penfluridol, a long-acting neuroleptic drug, as assayed by its behavioral actions.** Japanese Journal of Pharmacology (Kyoto). 26(6):693-702, 1976.

Penfluridol, a long-acting neuroleptic drug, was repeatedly given to rats well trained on the discriminated avoidance schedule (intertrial interval, 25 sec; warning duration, 5 sec), and accumulation of the effects was investigated by observing the behavioral changes. When penfluridol was orally given in a dose of 2 to 8mg/kg once daily for 10 consecutive days, the suppression of avoidance response was progressively enhanced until the 3rd to 4th day. But from the 4th day, the maximum level of suppression was maintained during the later medication. On its withdrawal, the avoidance response was gradually restored, returning to the initial level in 3 to 4 days. When 8mg/kg was given at 1 to 2 weeks after the withdrawal, the same suppression was observed as after single administration of the same dose. The progressive enhancement of suppression in the early half of the medication period evidently indicated the cumulative effect. The degree of suppression during the plateau showed a linear correlation with the dosage, and was estimated to be about 3.5times as high as in the corresponding single administration. 18 references. (Author abstract modified)

002491 Laschka, E.; Herz, A.; Blasig, J. Max-Planck-Institute, Neuropharmakologie, Kraepelinstrasse 2, D-8000 Munchen 40, Germany **Activity of the nigro-striatal dopaminergic system during precipitated morphine withdrawal investigated in rats with acute unilateral inactivation of the striatum.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 296(1):15-23, 1976.

The activity of the striatal dopamine system during precipitated morphine withdrawal was studied in rats using a model in which the striatum was unilaterally inactivated by the local injection of KCl. In naive rats dopamine agonists administered just prior to KCl induced ipsilateral turning or circling, while dopamine antagonists in the same situation caused contralateral turning. Withdrawal precipitated by morphine antagonists in dependent rats induced contralateral circling during unilateral inactivation of the striatum. This contralateral circling was only slightly enhanced by haloperidol, but strongly enhanced by a low dosage of apomorphine as well as by some weak dopamine agonists such as CB 154 or By 101. However, high doses of apomorphine completely reversed the withdrawal induced contralateral circling into ipsilateral circling. Other dopamine agonists, such as d-amphetamine, L-Dopa and piribedil, did not abolish the withdrawal induced contralateral circling, however, they caused the appearance of an additional ipsilateral circling. Other types of drugs which are known to intensify withdrawal induced jumping (desipramine, atropine, caffeine) enhanced contralateral circling. There are also other parallels between jumping and contralateral circling induced by withdrawal. The direction of naloxone induced asymmetric behavior during acute unilateral inactivation of the striatum suggests that striatal dopaminergic activity is reduced during precipitated withdrawal; the other results reported point to the possibility that extrastriatal dopaminergic mechanisms or different dopamine receptor types within the striatum are involved. 37 references. (Author abstract)

002492 Leander, J. David. Dept. of Pharmacology, School of Medicine, Swing Building, University of North Carolina, Chapel Hill, NC 27514 **Effects of promazine, chlorpromazine, d-amphetamine, and pentobarbital on treadle pressing by pigeons under a signalled shock-postponement schedule.** Journal of the Experimental Analysis of Behavior. 26(3):361-368, 1976.

The effects of promazine on treadle pressing to postpone the presentation of electric shock were studied in three pigeons, and the effects of chlorpromazine, d-amphetamine, and pentobarbital were studied in two of these pigeons. Each treadle press postponed electric shock for 20 seconds and presentation of a preshock stimulus for 14 seconds. Selected doses of both promazine and chlorpromazine increased the rates of treadle pressing in all birds. The response rate increases produced by promazine and chlorpromazine were due to increased conditional probabilities of treadle pressing both before and during the preshock stimulus. D-amphetamine (1 and 3mg/kg) slightly increased responding in one of the birds, but not to the extent that promazine or chlorpromazine did. In the other bird, the 10mg/kg doses of d-amphetamine increased shock rate but did not change response rate. Some doses of d-amphetamine increased the conditional probabilities of responding both in the absence of the preshock signal and during the preshock signal in both birds. Pentobarbital only decreased response rates and increased shock rates. 30 references. (Journal abstract modified)

002493 Maeda, Hisao. Department of Neuropsychiatry, Faculty of Medicine, Kyushu University, Fukuoka, Japan **Effects of psychotropic drugs upon the hypothalamic rage response in cats.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 30(4):539-546, 1976.

Effects of chlorpromazine (CPZ), haloperidol (HLP), pentobarbital (PTB), and diazepam (DZP) upon thresholds of the hypothalamically elicited rage response (i.e. directed attack and threat responses) were studied in chronic cats. All these drugs elevated the directed attack thresholds. CPZ and HLP elevated also the threat response thresholds and produced ataxia, but DZP did not show these effects. From these results, it is suggested that CPZ and HLP suppressed the amygdalo/ventromedial hypothalamic nuclear and cerebellar functions and DZP suppressed the afferent pathway of the directed attack. PTB showed intermediate effects between the above two groups. 23 references. (Author abstract)

002494 Malick, Jeffrey B. Biomedical Research Dept., ICI United States Inc., Wilmington, DE 19897 **Antagonism of isolation-induced aggression in mice by thyrotropin-releasing hormone (TRH).** Pharmacology Biochemistry and Behavior. 5(6):665-669, 1976.

To investigate the effects of thyrotropin-releasing hormone (TRH) on aggression in mice, a series of experiments were undertaken with isolation induced aggressive mice. TRH was shown to be an extremely potent antagonist of isolation induced aggression in male mice. The antifighting activity of TRH was selective in that it did not produce concurrent neurological impairment or significant alterations in spontaneous locomotor activity at antiaggressive doses. This activity of TRH appeared to be a direct affect on central nervous system structures since neither triiodothyronine nor any of the constituent amino acids of TRH antagonized aggression in isolated mice. The results are discussed in terms of the recent clinical effectiveness of TRH in some cases of mental illness

(e.g.,depression and schizophrenia). 31 references. (Author abstract modified)

002495 Manning, Frederick J. Walter Reed Army Institute of Research, Washington, DC 20012 **Role of experience in acquisition and loss of tolerance to the effect of delta9-THC on spaced responding.** Pharmacology Biochemistry and Behavior. 5(3):269-273, 1976.

The role of experience in acquistion of tolerance and loss of tolerance to the effects of delta9-tetrahydrocannabinol (THC) on spaced responding in albino rats was studied. Rats were given extensive training in spaced responding. During a 12 day hiatus from behavioral testing, half of the rats received daily intragastric doses of THC. On day 13, some of the animals received THC 3 hr prior to behavioral testing. The performance of the rats with 12 prior THC doses was no less affected than those with no previous THC administration, demonstrating that performance in the drug state can be a far more important determinant of tolerance than mere exposure to THC. Recovery of baseline performance occurred within 5 sessions, again with no effect of previous exposure. Drug administration was then discontinued for one week, during which some animals which had become tolerant to THC received training sessions, while others did not. Subsequent testing after a single dose of THC showed that only the animals receiving training sessions in the intervening week lost their previously acquired tolerance. It is suggested that experience appears to play an important role in loss of tolerance to THC as well as in acquisition of tolerance. 18 references. (Author abstract modified)

002496 Mayer, David J.; Price, Donald D. Medical College of Virginia, Virginia Commonwealth University, Richmond, VA 23298 **Central nervous system mechanisms of analgesia.** Pain. 4(2):379-404, 1976.

Recent advance in describing the anatomical, physiological, and neurohumoral substrates of neural systems which modulate pain perception is reviewed. Particular progress has been made in elucidating a neural system which can be activated by electrical stimulation of certain brainstem structures as well as by narcotic analgesic drugs. For this reason considerable emphasis has been placed on explaining its mechanisms. Recent evidence from behavioral observation with rats demonstrate that other neural systems also participate significantly in the modification of pain. 128 references.

002497 McKearney, James W. Worcester Foundation for Experimental Biology, 222 Maple Avenue, Shrewsbury, MA 01545 **Punishment of responding under schedules of stimulus-shock termination: effects of d-amphetamine and pentobarbital.** Journal of Experimental Analysis of Behavior. 26(2):281-287, 1976.

The effects of d-amphetamine and pentobarbital on punishment of responding under schedules of stimulus shock termination were investigated. Responding maintained in squirrel monkeys under 5 min fixed interval schedules of either food presentation or termination of a visual stimulus associated with electric shock delivery was suppressed by presenting an electric shock for every thirtieth response (punishment). In monkeys responding under the schedule of food presentation, d-amphetamine sulfate only further decreased punished responding, and pentobarbital sodium markedly increased punished responding, as expected from previous reports. In monkeys responding under the schedule of stimulus shock termination, however, the effects of the two drugs were opposite: d-amphetamine markedly increased punished responding, whereas pentobarbital only decreased responding. Thus, the effects of these drugs on punished responding were different depending on the type of event maintaining responding. These and previous results indicate that it may be misleading and inaccurate to speak of the effects of drugs on "punished responding" as though punishment were a unitary phenomenon. As with any behavior, the effects of drugs and other interventions on punished responding cannot be accurately characterized independently of the precise conditions under which the behavior occurs. 8 references. (Author abstract)

002498 Menon, M. K.; Clark, W. G.; Cannon, J. G. Psychopharmacology Research Laboratory, VA Hospital, Sepulveda, CA 91343 **Comparison of the dopaminergic effects of N-substituted aporphines.** Journal of Pharmacy and Pharmacology (London). 28(10):778-781, 1976.

Male mice pretreated with reserpine and administered various doses of N-substituted aporphines were monitored for activity to assess comparative dopaminergic effects. In doses effective in antagonizing reserpine sedation, the behavioral effects produced by the apomorphine analogues were quantitatively similiar to those of apomorphine. Reserpine induced ptosis was not antagonized by any of the tested compounds. Apomorphine and the ethyl and n-propyl derivatives showed marked antireserpine effects even at low doses. At a dose of 1 mg/kg, apomorphine and the n-propyl derivatives were equipotent, while the ethyl derivative was approximately 50% more active. It is suggested that the n-ethyl and n-propyl derivatives are twice as potent as apomorphine in reversing reserpine depression. 26 references.

002499 Miksic, Stephen; Smith, Nelson; Lal, Harbans. Dept. of Pharmacology and Toxicology, University of Rhode Island, Kingston, RI 02881 **Conditioning of discriminable stimuli produced by morphine.** Psychopharmacology Communications. 2(4):357-367, 1976.

At a symposium on the research aspects of drug induced discriminative stimuli (DS) conducted in connection with the annual meeting of the Behavioral Pharmacology Society, Durham, New Hampshire, in May 1976, a study in which mature male rats were injected with morphine or saline in an extended conditioning procedure using an external olfactory stimulus to investigate the conditioning of narcotic DS was reported. All rats readily learned to emit a response based upon morphine/saline discriminability. A stimulus systematically paired with each morphine injection and thereby with morphine action, acquired the ability to produce morphine DS formerly produced only by morphine. The conditional narcotic cue property had been learned by 100% of the animals who retained the original discrimination during the interruption of practice imposed by the conditioning procedure. It is suggested that the results support the hypothesis that a return to the original addiction environment can elicit a subjective narcotic high in an exaddict unless detoxification treatment includes a deconditioning process. 19 references.

002500 Miller, M. Ann; Bush, Maryann F.; Reid, Larry D. Bradley University, Peoria, IL 61606 **Addictive agents and intracranial stimulation: daily amphetamine and hypothalamic self-stimulation.** Bulletin of the Psychonomic Society. 8(4):333-335, 1976.

Twelve rats fixed with chronically indwelling electrodes for stimulation of the lateral hypothalamus were used to test for the effects of daily doses of amphetamine. The rate of pressing for brain stimulation was observed 1, 4, and 23 h

after injections in 5 min sessions. These doses did not reliably increase selfistimulation rates during the times of testing. During the 5 days following termination of injections, pressing rates of rats receiving amphetamine were slightly less than those of rats receiving a placebo. 11 references. (Author abstract)

002501 Misslin, R.; Hinschberger, A.; Maitre, M.; Ciesielski, L. Laboratorie de Psychophysiologie, Universite Louis Pasteur, 7 Rue de Universite, F-67000 Strasbourg, France **Effects of 2-propyl 2-pentenoic acid on the acquisition of conditioned behavior with negative reinforcement in mice.** Psychopharmacology (Berlin). 50(1):53-54, 1976.

The action of 2-propyl 2-pentenoic acid (PP) on the acquistion of conditioned avoidance reactions in mice was studied. PP (6mg/kg) had a facilitating action on the acquistion of conditioned avoidance reactions. This effect of PP is correlated with increase of the level of brain gamma-aminobutyric acid, following administration of PP. 8 references. (Author abstract)

002502 Modianos, Doan T.; Delia, Helen; Pfaff, Donald W. Rockefeller University, New York, NY 10021 **Lordosis in female rats following medial forebrain bundle lesions.** Behavioral Biology. 18(1):135-141, 1976.

The effects of medial forebrain bundle lesions in three testing situations in which a facilitation of feminine sexual behavior might be demonstrated was studied and presented as follows: 1) increased responsiveness to a constant estrogen dosage; 2) decreased estrogen thresholds; and 3) increased duration of receptivity. Ovariectomized rats given weekly injections of estrogen and progesterone which were relatively unresponsive during preoperative testing received bilateral medial forebrain bundle (MFB) lesions. Postoperative lordosis quotients were significantly elevated. MFB lesion and sham lesion rats were tested for responsiveness to decreasing doses of estrogen, and it was demonstrated that lesions had no significant effect. MFB lesions significantly increased the duration of receptivity following single injections of estrogen and progesterone. These results suggest that under some conditions the MFB may play a role in the suppression of lordosis. 15 references. (Author abstract modified)

002503 Mogilnicka, E.; Klimek, V.; Golembiowska-Nikitin, K. Institute of Pharmacology, Polish Academy of Sciences, 12 Smetna Str., 31-344 Krakow, Poland **Effect of nomifensine on central 5-hydroxytryptamine neurons.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 294(Supplement):R16, 1976.

In a paper presented at a pharmacology meeting in Hannover, Germany, on September 14-17, 1976, the effects in rats of nomifensine (NF), an antidepressant drug inhibiting dopamine uptake, on central serotonergic structures were reported. NF induces changes of 5-hydroxytryptamine (5-HT) and 5-hydroxyindoleacetic acid levels in the whole brain as well as in the midbrain, hippocampus, and striatum regions, and it stimulates the hindlimb flexor reflex of spinal rat. It was concluded that NF activates central 5-HT neurons both directly and indirectly via stimulation of dopamine receptors. (Author abstract modified)

002504 Moja, Egidio A.; Stoff, David M.; Gillin, J. Christian; Wyatt, Richard Jed. Division of Special Mental Health Research, IRP, NIMH, Saint Elizabeth's Hospital, Washington, D.C. **Dose-response effects of beta-phenylethylamine on stereotyped behavior in pargyline-pretreated rats.** Biological Psychiatry. 11(6):731-742, 1976.

The dose response and the time course effect of beta-phenylethylamine (PEA), a naturally occurring sympathomimetic amine whose presence has been demonstrated in animal and human brains, on stereotyped behavior and motor activity was studied in male rats pretreated two hours earlier with pargyline. Stereotyped behavior, defined as repetitive, nongoal directed head movements and sniffing, and changes in motor activity were observed immediately after injection of PEA for a 1 hr, period. With increasing doses of pargyline pretreatment, PEA produced, in a dose response relationship, progressively more stereotyped behavior accompanied by increased motor activity. Without pargyline pretreatment, only the highest experimental dose of PEA induced behavioral changes. Stereotyped behavior and increased motor activity had an onset at 4 to 6 min after the injection of DEA, peak at 10 to 30 min, and gradual decline in the next 10 to 20 min. These results are discussed in terms of a possible relationship with the degree of inhibition of Type A and Type B monoamine oxidase caused by the different doses of pargyline. 31 references. (Author abstract modified)

002505 Moja, Egidio A.; Stoff, David M.; Gillin, J. Christian; Wyatt, Richard Jed. Laboratory of Clinical Psychopharmacology, National Institute of Mental Health, St. Elizabeths Hospital, Washington, DC 20032 **Neuroleptics attenuate stereotyped behavior induced by beta-phenylethylamine in rats. (Unpublished paper).** Bethesda, MD, NIMH, 1976. 15 p.

The effects of neuroleptic drugs on beta-phenylethylamine (PEA) induced stereotyped behavior were studied in rats pretreated with pargyline. PEA induced stereotyped behavior consisting of continuous head movements and sniffing associated with increased motor activity. Pretreatment with haloperidol, pimozide, chlorpromazine or clozapine attenuated the effects of PEA in a dose dependent manner. Diazepam had no significant effect on either stereotypy or hyperactivity. The order of effectiveness of the neuroleptics in blocking PEA induced stereotypy paralleled very closely the reported order of neuroleptic blockade of striatal dopaminergic receptors. The data is consistent with the hypothesis that PEA induces stereotyped behavior through a dopaminergic mechanism. 44 references. (Author abstract modified)

002506 Molander, L.; Randrup, A. AB Ferrosan, Celciusgatan 35, Malmo, Sweden **Effects of thymoleptics on behavior associated with changes in brain dopamine. II. Modification and potentiation of apomorphine-induced stimulation of mice.** Psychopharmacology (Berlin). 49(2):139-144, 1976.

The effects of imipramine, desipramine, cholorimipramine, amitriptyline, FG-4963, atropine, scopolamine, benztropine, amphetamine, pipadrol, and clonidine on apomorphine induced gnawing behavior were studied in mice. The antidepressant drugs (including the experimental substance FG-4963) and clonidine produce the strongest potentiation of apomorphine induced biting, while the anticholinergic drugs elicit a weaker response and the stimulant drugs produce no significant response. Possible mechanisms by which the various classes of drugs may exert their effects on apomorphine induced gnawing are discussed. It is not likely that the thymoleptic drugs (imipramine, desipramine, chlorimipramine and amitriptyline) act by the same mechanism as do the anticholinergic drugs, but definite conclusions concerning the mechanisms by which thymoleptics potentiate gnawing cannot be drawn at this time. The effect of the thymoleptics is not abolished by emptying of amine stores. It is suggested that these drugs facilitate the access of apomorphine to the dopamine receptors. 29 references.

002507 Moniuszko-Jakoniuk, J.; Wisniewski, K. Department of Pharmacology, Institute of Physiology and Biochemistry, Medical School, 15-222 Bialystok, Poland **Interaction of bradykinin with dopaminergic receptors in the CNS.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 294(Supplement):R15, 1976.

In a paper presented at a pharmacology meeting in Hannover, Germany, on September 14-17, 1976, studies on the influence of kinins on the actions of compounds stimulating and blocking central catecholamine receptors in rats were described. The following compounds were used: nialamide, noradrenaline, dopamine, 1-3-dimethyl-5-aminoadamantan (D145), L-DOPA, apomorphine, phentolamine, propranolol, haloperidol, and spiroperidol. It was found that bradykinin potentiates the action of all the studied psychostimulatory compounds and of propranolol. It does not change the action of phentolamine, but it decreases catalepsy after haloperidol. It is concluded that bradykinin effects depend on the interaction of this peptide with dopaminergic receptors. (Author abstract modified)

002508 Moore, John W.; Goodell, Nancy A.; Solomon, Paul R. Department of Psychology, Middlesex House, University of Massachusetts, Amherst, MA 01002 **Central cholinergic blockade by scopolamine and habituation, classical conditioning, and latent inhibition of the rabbit's nictitating membrane response.** Physiological Psychology. 4(3):395-399, 1976.

Rabbits injected with scopolamine hydrobromide were contrasted with control animals injected with scopolamine methylbromide or saline in terms of habituation of the unconditioned nictitating membrane response (NMR), classical defensive conditioning, and latent inhibition using auditory and visual conditioned stimuli. Scopolamine hydrobromide disrupted classical conditioning in comparison with drug controls, but had no adverse effects on habituation of the unconditioned reflex or on latent inhibition. The drug also raised thresholds of the auditory (but not visual) CS for eliciting the conditioned NMR. Results were discussed in terms of presumed cholinergic/limbic system involvement in Pavlovian conditioning and inhibition. 14 references. (Author abstract)

002509 Nabeshima, Toshitake; Nakamura, Yoshiki; Tatsuyama, Tsutomu. no address **The effects of analgesics on the conditioned behavior of rats (II).** Annual of Animal Psychology (Tokyo). 26(1):48, 1976.

In a summary of a paper read to the 36th Symposium of Japanese Animal Psychologists held in June 1976 at Osaka University, the results of an experiment testing the analgesic effects of the psychotropic drugs, methamphetamine (MA) and chlorpromazine on the conditioned behavior of rats are reported. Rats were on a DRL schedule and the analgesic effects of MA were compared with those of other drugs known to act on the central nervous system. MA and diazepam (2mg/kg), as well as morphine (20mg/kg), produced an increasing frequency of bar pressing activity, and reduced food taking activity. Chlorpromazine in 10mg/kg doses reduced both activities. The drugs difenamizol, aminopyrine, and chlorpromazine in smaller doses all had no noticeable effect on bar pressing, but did reduce food taking. Small dosages of aminopyrine, morphine, difenamizol, as well as aspirin had no behavioral effects.

002510 Nishikawa, Tadashi; Kajiwara, Yumiko; Kohno, Yasuko; Sano, Takayasu; Tanaka, Masatoshi; Nagasaki, Nobuyuki. Department of Pharmacology, Kurume University School of Medicine, Kurume 830, Japan **Social isolation induced behavioral changes under intense stimuli and the biochemical mechanism.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):105P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March 1976, a study of possible neurobiochemical alterations in rats reared in social isolation which could affect behavior was reported. Male Wistar rats were isolated for 12 weeks immediately after weaning and were exposed periodically to electric foot shock of various intensities. Immediately after foot shock, the animals were decapitated and brain monoamines and their metabolites were measured. The frequency of shock elicited jumping in isolated rats was lower than that in group animals; the difference between the two groups was greatest with the most intense shock. This behavioral effect was diminished by placing isolated rats into grouped housing. Noradrenaline turnover, but not serotonin turnover, was increased in both isolated and grouped animals. Methamphetamine (a catecholaminergic neuron stimulant) and chlorpromazine (a catecholaminergic neuron blocker) were administered to both isolated and grouped rats and were found to produce different effects on shock induced jumping in the two groups. It is suggested that the behavior of isolated rats may be the result of a changed brain macromolecular composition of catecholaminergic neurons. (Author abstract modified)

002511 Noble, Adele B.; McKinney, William T., Jr.; Mohr, Carole; Moran, Elaine. University of Wisconsin, Madison, WI 53706 **Diazepam treatment of socially isolated monkeys.** American Journal of Psychiatry. 133(10):1165-1170, 1976.

The effects of diazepam treatment on four rhesus monkeys which were reared for the first 8 months of their life in social isolation are reported. One animal died during the isolation period, but the other three were treated with diazepam in an isolation chamber, in their home cages, and in a playroom testing situation. Diazepam significantly decreased the self-disturbance behaviors of two subjects, and there was even the appearance of some social behaviors, although they were limited and not of the same quality as in nonisolated animals. The implications of this data for the understanding of the significance of social isolation syndrome in monkeys were discussed as a model for human psychoses. 10 references. (Journal abstract modified)

002512 Ogata, Hiroko; Gomita, Yutaka. Department of Pharmacology, Dai-ichi College of Pharmaceutical Sciences, Fukuoka 815, Japan **Effects of various psychotropic drugs on intracranial self-stimulation behavior in rats.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):40P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study of the effects of various psychotropic drugs on the low rate (LR) and high rate (HR) lever pressing responses of lateral hypothalamic self-stimulation behavior of rats was reported. The LR response was markedly reduced by 2mg/kg chlorpromazine; the LR response was completely suppressed and the HR response was decreased to 50% of control by a dose of 10mg/kg. The LR response was markedly increased by diazepam in doses of 1mg/kg to 10mg/kg, but was suppressed with large doses of 60mg/kg to 80mg/kg. The HR response was not changed by diazepam in doses of 40mg/kg to 180mg/kg. As in the case of diazepam, the LR response was increased with smaller doses of triazolam, ID-690 ((5-0-chlorophenyl)-1-methyl-7-nitro-1, 3-dihydro-2h-1, 4-benzodiazepine-2-one) and prazepam, but was suppressed by large doses; the HR response was not affected by these drugs even in large doses. Amitriptyline increased the LR response in a dose of 40mg/kg

but suppressed it in a dose of 80mg/kg. It is suggested that the LR response of this self-stimulation is useful for the evaluation of various psychotropic drugs, especially those having an antianxiety effect. (Author abstract modified)

002513 Ogawa, Haruyoshi; Higuchi, Yoichiro; Okamoto, Michiko; Tadokoro, Sakutaro. Behavior Research Institute, School of Medicine, Gunma University, Maebashi 371, Japan **Effects of intermittent administration of d-amphetamine on locomotor activity and heart rate in rats.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):36P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study of the effects of weekly administration of various doses of d-amphetamine on locomotor activity and heartrate in rats was reported. Group A was tested for the effect of weekly treatments of the drug in the test chamber. Group B was used for observation of the effects in the test chamber one week after 10 weekly drug treatments in their home cages. On the first treatment in group A, locomotor activities were accelerated in parallel with increased doses of d-amphetamine. In the 0.5mg/kg group, the effect was gradually enhanced, but in the 1.0mg/kg group, a similarly enhanced effect was observed up to the sixth test and then a diphasic pattern of the effect became prominent. In the 2.0mg/kg group, after several treatments, a multiphasic pattern of the effect developed together with abnormal stereotyped behavior. The heart rates showed no change in any group in the 1st test. However, in 1.0and 2.0mg/kg groups, the heartrates decreased markedly according to the repetitions of test from about 5 to 120 min after the drug treatment. The more prominent the diphasic or multiphasic accelerative effect on the locomotor activity, the more remarkable was the depression of heartrates. In Group B, no change was observed in locomotor activity or in heartrate. (Author abstract modified)

002514 Ohi, Shuzo. Tokyo Medical and Dental University, Tokyo, Japan **The effect of ometine on learned behavior in the Wakin goldfish.** Annual of Animal Psychology (Tokyo). 26(1):49, 1976.

In a summary of a paper read to the 36th Symposium of Japanese Animal Psychologists held in June 1976 at Osaka University, results of an experiment to test the behavioral effects of the protein synthesis blocking drug, ometine, on goldfish are reported. Goldfish were given 40 go/no go trials in a shuttle box and were considered trained after 34 successful trials. The next day 100mg of ometine in distilled water were injected into the cranium. On the day of injection, the ometine group showed markedly inferior performance, but on the following day when no more ometine was administered, the performance of the two groups was the same. It was concluded that ometine had a transitory effect on performance, but that that effect did not have anything to do with its protein synthesis blocking effects, and it was suggested that protein blocking did not have any effect on prelearned habits.

002515 Oka, Makoto; Kamei, Chiaki; Shimizu, Masanao. Research Laboratories, Dainippon Pharmacuetical Co., Ltd., Suita, Osaka 564, Japan **Effects of neuroleptic drugs on the avoidance response after pretreatment with alpha-methyltyrosine or p-chlorophenylalanine.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):36P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, March, 1976, a study of the effects of neuroleptic drugs on the avoidance response of rats after pretreatment with alpha-methyltyrosine (AMT) or p-chlorophenylalanine (PCPA) was reported. The operant conditioning procedure used was composed of the concurrent approach and avoidance schedules in a Skinner box. Chlorpromazine, perphenazine, haloperidol and oxypertine inhibited operant behavior after pretreatment with AMT. Such potentiating effects by AMT were not observed with diazepam and nortriptyline. PCPA pretreatment did not influence suppressive effects on the operant behavior by any drug used. The effects of various drugs on the one way active avoidance procedure in mice were also studied. Chlorpromazine, perphenazine, haloperidol, trifluperidol, clozapine and oxypertine showed a suppressive effect, which was markedly potentiated by AMT. Diazepam, clonidine, phenoxybenzamine, phentolamine, arecoline and physostigmine also had a suppressive effect on the avoidance response, but the effect of these drugs was not influenced by pretreatment with AMT. It is suggested that the suppressive effects of neuroleptics on conditioned behavior are selectively potentiated by AMT, and not influenced by PCPA. (Author abstract modified)

002516 Okamoto, Michiko; Rosenberg, Howard C.; Boisse, Norman R. Department of Pharmacology, Cornell University Medical College, 1300 York Avenue, New York, NY 10021 **Withdrawal characteristics following chronic pentobarbital dosing in cat.** European Journal of Pharmacology (Amsterdam). 40(1):107-119, 1976.

Withdrawal characteristics following chronic pentobarbital dosing in cats were studied. Sixty three cats were made physically dependent by maximally tolerable dosing with sodium pentobarbital. After 5 wk of chronic treatment each animal was placed in an activity monitoring cage and observed for signs of barbiturate abstinence. Electroencephalographic monitoring of sleep/wake cycles was performed in five cats. Most withdrawal signs appeared in 12 hr to 18 hr and intensified rapidly. Primary motor and autonomic effects were tremors, twitching, shaking, impaired motor coordination, decreased motor activity, piloerection, pupillary dilatation and startle response. Twenty six animals (41%) died during withdrawal, usually during or immediately following grand mal type seizures. The most significant behavioral effects were passivity, overly affectionate behaviors and apprehensiveness. These effects usually began about 24 hrs following withdrawal and reached a maximum between 1 and 4 days. EEG monitoring showed significant changes in sleep patterns with a complete lack of sleep on the 2nd and 3rd day following withdrawal and a normal state reached by day 7. It is posited that this approach will render a more accurate quantitation of physical dependence through categorizing as many withdrawal signs as possible. 30 references. (Author abstract modified)

002517 Overton, Donald A. Temple Medical School, Eastern Pennsylvania Psychiatric Institute, Philadelphia, PA 19129 **Discriminable effects of benzodiazepines.** Psychopharmacology Communications. 2(4):339-343, 1976.

At a symposium on the research aspects of drug induced discriminative stimuli conducted in connection with the annual meeting of the Behavioral Pharmacology Society, Durham, New Hampshire, in May 1976, a study of the discriminable effects of benzodiazepines in rats was reported. In a shock/escape T-maze task, rats rapidly discriminated diazepam, flurazepam, and chlordiazepoxide from no drug. The discriminable effects of these benzodiazepines were not completely interchangeable with those of barbiturate anesthetics. The dose/response curve for diazepam asymptoted over the range 15mg/kg to 100mg/kg, whereas dose/response curves for flurazepam and chlordiazepoxide were more linear.

The possible production of state dependency and discrimination in human subjects by benzodiazepines is briefly discussed. 6 references. (Author abstract modified)

002518 Patkina, Nadezda A.; Lapin, Izyaslav P. Department of Pharmacology, First Leningrad Pavlov Medical Institute, 197089 Leningrad, USSR **Effect of catecholaminergic drugs on systems of reward and punishment in experiments on cats.** Pharmacology Biochemistry and Behavior. 5(3):247-252, 1976.

The effects of catecholaminergic drugs on systems of reward and punishment were studied in cats to assess the roles of the monoamines in the reward systems. Injection of amantadine or DOPA produced inhibition of both self-stimulation and negative reinforcing effects of stimulation of the hypothalamus. After injection of l-DOPA in cats pretreated with seryl-trihydroxybenzylhydrazine (Ro 4-4602), an inhibitor of peripheral decarboxylase, or disulfiram, a dopamine-beta-hydroxylase inhibitor, the inhibitory action on the reinforcing system was enhanced. Amphetamine activated both reward and punishment systems. The data supports an inhibitory function of dopamine in systems of reinforcement and of an activating function of noradrenaline in these systems. 17 references. (Author abstract modified)

002519 Peterson, D. W.; Laverty, R. Deparment of Pharmacology, University of Otago, Medical School, Dunedin, New Zealnd **Operant behavioural and neurochemical effects after neonatal 6-hydroxydopamine treatment.** Psychopharmacology (Berlin). 50(1):55-60, 1976.

In a study of the behavioral and neuorchemical effects of 6-hydroxydopaimine (6-OHDA), newborn rats were treated at 1 and 2 days after birth with 100mg/kg 6-OHDA. Testing on several operant behavioral tasks was begun at 6 months of age. On a fixed-ratio 30 (FR30) schedule of food reinforcement, the neonatal 6-OHDA treated rats responded at a significantly higher rate. Further analysis of the FR30 response pattern indicated that the higher rate was due to a decrease in the amount of time spent pausing after the receipt of each reinforcer. The 6-OHDA treatment failed to alter the rat's behavior during the extinction of the FR30 response and on the progressive ratio or variable interval schedules of food reinforcement. Biochemical analysis of several brain areas at 9 months of age showed a decrease in noradrenaline (NA) levels in the cerebral cortex and hippocampus, while in the pons medulla NA content was doubled. The tyrosine hydroxylase activity in these same brain areas was not significantly altered, but there appeared to be some decrease in the activity of this enzyme in the hippocampus. Comparisons of the operant behavioral effects seen after various lesioning procedures in this and other studies suggest the effects on fixed-ratio performance are a result of destruction of noradrenergic neurons in the hippocampus and/or the apparent regeneration of neurons in the pons medulla. 19 references. (Author abstract modified)

002520 Poddubiuk, Zbigniew M. Department of Pharmacology, School of Medicine, Jaczewskiego 8, 20-090, Lublin, Poland **A comparison of the central actions of prostaglandins A1, E1, E2, F1alpha, and F2alpha in the rat: I. Behavioral, antinociceptive and anticonvulsant actions of intraventricular prostaglandins in the rat.** Psychopharmacology (Berlin). 50(1):89-94, 1976.

The effect of prostaglandins (PGs) A1, E1, E2, F1alpha and F2alpha administered intraventricularly at doses of 0.02-4.0microg/rat were studied in some behavioral, antinociceptive, and anticonvulsant tests in rats. Acute toxcity, motor coordination, locomotor activity, exploratory behavior, body temperature, and analgesic activity were evaluated and analysed by means of the Student's t-test. Results indicated that exploratory and locomotor activity were decreased by all PGs except A1 and F2alpha which had no effect on locomotor activity. All PGs studied, except A1, induced hyperthermia and afforded protection in the hot plate analgesic test and against maximal electroschock seizures. 35 references. (Author abstract)

002521 Protais, P.; Costentin, J.; Schwartz, J. C. Laboratoire de Pharmacodynamie et Physiologie, U.E.R. de Medecine et Pharmacie, 49, Rue Maulevrier, F-7600 Rouen, France **Climbing behavior induced by apomorphine in mice: a simple test for the study of dopamine receptors in striatum.** Psychopharmacology (Berlin). 50(1):1-6, 1976.

A simple test based on behavioral response for the study of dopamine receptors in the striatum of mice is described. It is noted that mice treated with low doses of apomorphine adopt a vertical position along the walls of their cage. This peculiar behavior appears to be elicited by stimulation of dopamine receptors in the striatum: it is suppressed after coagulation of this structure, while it is facilitated when these receptors are made hypersensitive by previous treatments with 6-hydroxydopamine or haloperidol; on the other hand, it is not modified by coagulation of the nucleus accumbens. The relative efficacy of various agonists and antagonists of dopamine receptors were determined on this test after establishing optimum conditions to obtain a reliable dose/response relationship. It is suggested that this sterotyped climbing behavior represents a convenient means to assess the stimulation of striatal dopamine receptors in mice.

002522 Pycock, C. J.; Horton, R. W. Department of Neurology, King's College Hospital Medical School, Denmark Hill, London SE5 8AF, England **Possible GABA-mediated control of dopamine-dependent behavioural effects from the nucleus accumbens of the rat.** Psychopharmacology (Berlin). 49(2):173-178, 1976.

The effect of elevating gamma-aminobutyric acid (GABA) levels in the nucleus accumbens on various dopamine dependent behaviors was studied in rats. Injection into the nucleus accumbens of the GABA-transaminase inhibitor ethanolamine orthosulfate (EOS) produced a maximal increase in GABA concentrations on day 1, a notable increase in GABA concentrations on day 3, and a return to normal by day 7. Animals exhibited normal spontaneous activity and exploratory behavior in a hole board apparatus. When mesolimbic GABA levels were maximal (day 1), systemic amphetamine did not induce increased locomotor activity, and dopamine (injected directly into the nucleus accumbens), did not produce hyperactivity but apomorphine induced stereotyped behavior was not affected. A possible GABA mediated control of dopaminergic mechanisms in the nucleus accumbens is suggested, and the possible site of interaction discussed. 30 references. (Author abstract modified)

002523 Quock, R. M.; Horita, A. Department of Pharmacology, University of Washington School of Medicine, Seattle, WA 98195 **Differentiation of neuropharmacological actions of apomorphine and d-amphetamine.** Pharmacology Biochemistry and Behavior. 5(6):627-631, 1976.

To compare the extent of serotonergic involvement in the neuropharmacological activities of apomorphine and d-amphetamine, a series of experiments were undertaken with drug free and drug pretreated male rabbits. The dopaminergic

agonists apomorphine and d-amphetamine elicit hyperthermic, hyperkinetic and sterotypic responses in the rabbit. Apomorphine induced hyperthermia was antagonized by p-chlorophenylalanine, cyproheptadine, and cinanserin and was restored in p-chlorphenylelanine, pretreated rabbits by regeneration of central serotonin levels. d-Amphetamine induced hyperthermia was reduced by p-chlorophenylalanine, restored in p-chlorophenylalanine, pretreated animals by regeneration of central serotonin levels; and was uninfluenced by cyproheptadine and cinanserin. Apomorphine induced locomotor stimulation was unaltered by serotonergic antagonists. However, these same doses of antiserotonergio agents all markedly reduced d-amphetamine induced hyperkinesia. Serotonergic antagonists also failed to affect apomorphine induced compulsive gnawing but did significantly enhance d-amphetamine induced compulsive gnawing. It is concluded from these data that the neuropharmacological activities of apomorphine and d-amphetamine in the rabbit differ in their dependence upon central serotonergic mechanisms. 23 references. (Author abstract modified)

002524 Risner, Marc E.; Jones, B. E. National Institute on Drug Abuse, Division of Research, Addiction Research Center, Lexington, Kentucky **Characteristics of unlimited access to self-administered stimulant infusions in dogs.** Biological Psychiatry. 11(5):625-634, 1976.

Drug naive dogs were given unlimited access to response contingent intravenous infusions of either d-amphetamine, phenmetrazine, or methylphenidate. A regular cycle of drug intake interspersed with periods of voluntary abstinence was seen. During the drug self-administration phases there was a marked increase in locomotor behavior and stereotypy along with a decrease in bodyweight; the rest periods were characterized by minimal activity. These results are similar to those observed when humans engage in high dose intravenous abuse of psychomotor stimulants. It is generally believed that stereotypy occurs following intense activation of dopamine systems in the corpus striatum since amphetamine induced stereotypy can be attenuated if the animal is pretreated with alpha-methyl-p-tyrosine, but pretreatment with diethyldithiocarbamate has no behavioral effects. Also, it has been shown that haloperidol antagonizes the effects of amphetamine induced stereotypy. 23 references. (Author abstract)

002525 Rodriguez-Sierra, Jorge F.; Naggar, Auri N.; Komisaruk, Barry R. Institute of Animal Behavior, Rutgers University, Newark, NJ 07102 **Monoaminergic mediation of masculine and feminine copulatory behavior in female rats.** Pharmacology Biochemistry and Behavior. 5(4):457-463, 1976.

The role of dopamine (DA) and serotonin (5-hydroxytryptamine, 5-HT) in the control of copulatory behavior in female rats was investigated. Ovariectomized animals treated with testosterone propionate (TP) and the 5-HT synthesis inhibitor para-chlorophenylalanine (PCPA) showed more masculine copulatory behavior (including the ejaculatory pattern) than did animals receiving either TP or PCPA alone. The monoamine oxidase inhibitor pargyline antagonized, rather than potentiated, the facilitatory effect of PCPA. The DA receptor stimulant apomorphine did not increase masculine copulatory behavior in TP treated females. The results suggest a 5-HT mediated inhibition of masculine copulatory behavior in female rats. Females receiving TP, PCPA and pargyline, TP and pargyline, or TP and apomorphine all displayed lordosis in response to mounting by male rats but those receiving TP, PCPA or pargyline individually or in any other combination did not. These results are consistent with the hypothesis of a noradrenergic facilitatory system for lordotic behavior. The responses in the apomorphine group are discussed in terms of a possible role for low level dopaminergic stimulation in facilitating lordosis. 39 references. (Author abstract modified)

002526 Rosecrans, J. A.; Chance, W. T.; Schechter, M. D. Dept. of Pharmacology, Medical College of Virginia, Richmond, VA 23298 **The discriminative stimulus properties of nicotine, d-amphetamine and morphine in dopamine depleted rats.** Psychopharmacology Communications. 2(4):349-356, 1976.

At a symposium on the research aspects of drug induced discriminative stimuli conducted in connection with the annual meeting of the Behavioral Pharmacology Society, Durham, New Hampshire, in May 1976, a study of the discriminative stimulus properties of nicotine, dextroamphetamine, and morphine in dopamine (DA) depleted rats was reported. Rats depleted of dopamine by neonatal administration of 6-hydroxydopamine (6-OHDA) (DA rats), learned to discriminate both morphine and d-amphetamine as rapidly as controls, and exhibited similar sensitivity when dose generalization studies were conducted. DA rats appeared to tolerate higher doses of the same drug better than controls indicating that they were more tolerant to behavioral disruption. It is suggested that the behavioral disruption usually seen with these drugs may, in part, be due to an effect on DA neurons. DA rats had more difficulty learning to discriminate nicotine than controls. The peripherally injected nicotine stimulus generalized to hippocampal injections in controls but this was not observed in DA rats. These data suggest that part of nicotine's discriminative stimulus properties may be contingent upon the integrity of a Hp-DA connection. 6 references. (Author abstract modified)

002527 Rosenfeld, J. Peter; Vickery, Jon L. Cresap Neuroscience Laboratory, Northwestern University, Evanston, IL 60201 **Differential effect of morphine on trigeminal nucleus versus reticular aversive stimulation: independence of negative effects from stimulation parameters.** Pain. 4(2):405-416, 1976.

The differential effect of morphine on trigeminal nucleus vs reticular aversive stimulation with focus on the independence of negative effects from stimulation parameters is discussed. Electrodes were implanted in mesencephalic, pontine, and bulbar reticular formation, and in spinal trigeminal nucleus and tract of rats. Central and peripheral aversive response thresholds were studied under normal conditions and with morphine. Peripherally elicited aversive reactions were assessed. Centrally elicited aversive reaction thresholds were in all cases based on unconditioned behavioral distress signs and confirmed in some cases with avoidance learning. Morphine elevated the unconditioned aversive reaction threshold for brain stimulation in the trigeminal complex and for peripheral aversive stimulation, but failed to affect the thresholds for reticular brain stimulation. The failure to affect reticular thresholds was independent of stimulation frequency. Thresholds for 5 and 200 Hz sinusoidal stimulation were both unaffected as were previously reported thresholds with 333 Hz pulsatile stimulation. Trigeminal nucleus and tract stimulation were affected in similar degrees. 19 references. (Author abstract modified)

002528 Rossi, Nello A.; Reid, Larry D. Bradley University, Peoria, IL 61606 **Affective states associated with morphine injections.** Physiological Psychology. 4(3):269-274, 1976.

The hypothesis that morphine injections produce a positive affective state and that the positive state occurs at times when self-stimulation is facilitated is examined. Rats were placed in

one compartment of an alley for 30 min at 1, 4.5, and 7 h after morphine or saline injections on 3 consecutive days. On the 4th day, rats were allowed access to the entire alley while time spent in the compartment where they had experienced the effects following injections was tabulated. This 4 day cycle of training and testing was repeated four times. On test days, rats experiencing morphine in a compartment during times corresponding to morphine facilitation of self-stimulation, and at 1 hr after injections, spent more time in that compartment than rats experiencing saline. 25 references. (Author abstract modified)

002529 Sanger, D. J.; Blackman, D. E. Dept. of Psychology, University of Birmingham, P. O. Box 363, Birmingham B15 2TT, England **The effects of d-amphetamine on the temporal control of operant responding in rats during a preshock stimulus.** Journal of the Experimental Analysis of Behavior. 26(3):369-378, 1976.

The effects of d-amphetamine on the temporal control of operant behavior during a preshock stimulus were investigated among six male, hooded rats. The operant behavior of the subjects was maintained by a random interval schedule of reinforcement. Three minute periods of noise were superimposed on this behavior, each period ending with the delivery of an unavoidable shock. Overall rates of responding were generally lower during the periods of noise than in its absence (conditioned suppression). These suppressed response rates also exhibited temporal patterning, with responding becoming less frequent as each noise period progressed. The effects of d-amphetamine on this behavioral baseline were then assessed. In four animals the relative response rates during the noise and in its absence suggested that the drug produced a dose related decrease in the rates of responding in the absence of the preshock stimulus, rather than to an increase in response rates during the stimulus. Temporal patterning in response rates during the preshock stimulus was abolished, an effect that was interpreted in terms of rate dependent effects of d-amphetamine. This study thus extends rate dependent analyses of the effects of amphetamines to the patterns of operant behavior that occur during a preshock stimulus, and which have been discussed in terms of the disrupting effects of anxiety on operant behavior. 42 references. (Journal abstract modified)

002530 Sato, Takashi; Kobayashi, Masafumi; Sato, Mikio. Department of Pharmacology, Nihon University School of Dentistry, Tokyo 101, Japan **Influence of adrenalectomy on stereotypy and brain tyramine uptake in methamphetamine-treated rats -- effects of L-DOPA, MAOI and alpha-MMT, in particular.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):34P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study of the influence of adrenalectomy on stereotyped behavior and brain tyramine uptake in methamphetamine treated rats was reported. The tyramine uptake of all adrenalectomized and sham operated groups pretreated with saline solution was increased 5 min after the methamphetamine injection and afterwards decreased or remained steady. Contents of noradrenaline (NA) increased in safrazine pretreated animals 5 min. after the methamphetamine injection and then decreased considerably. Adrenalectomized animals and safrazine, alpha-methyl-m-tyrosine and L-DOPA pretreated groups displayed almost no stereotyped licking or biting activity. Although pretreatment with drugs affecting brain catecholamine levels produced the same effects as adrenalectomy on methamphetamine stereotypies, the dynamic aspects of tyramine uptake and NA content in the brain did not correlate with such effects. (Author abstract modified)

002531 Sbordone, Robert Joseph. University of California, Los Angeles, CA 90024 **A rat model of violent attack behavior. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-22213 HC$15.00 MF$8.50 108 p.

Four experiments were conducted on shock elicited aggression in rats, and a rat model of violent attack behavior was developed. Experiment 1 examined whether shock was necessary to initiate violent attack behavior in mescaline treated Ss. Experiments 2 and 3 assessed whether the behavior of mescaline treated rats could elicit violent attack behavior in untreated rats. Experiment 4 determined if violent attack behavior was due to CNS excitation and a restriction of upright fighting postures. Three hypotheses were formulated to explain the results: 1) mescaline released aggressive behavior from species typical inhibitory control; 2) the violent behavior was due to mescaline's restriction of upright posture; and 3) the behavior was due to mescaline's disruption of social signals that regulate the topography of aggressive behavior. The findings were most in agreement with the third hypothesis and suggested that the reported differences in aggressiveness between wild and laboratory rats may reflect the effectiveness of their respective social signalling systems. When combined with previous data, the mescaline induced attack behavior paradigm may serve as an experimental rat model for investigating the causes or treatment of violent behavior in the laboratory. (Journal abstract modified)

002532 Schreiber, Henry; Bell, Robert; Conely, Lynn; Kufner, Michael; Palet, James; Wright, Linda. Department of Psychology, Texas Tech University, PO Box 4100, Lubbock, TX 79409 **Diminished reaction to a novel stimulus during amphetamine withdrawal in rats.** Pharmacology Biochemistry and Behavior. 5(6):687-690, 1976.

To determine whether reaction to a novel stimulus is diminished in a dose dependent fashion following 8 consecutive days of d-amphetamine administration, 32 male rats were injected with saline, 0.5, 2.5, or 5.0mg/kg of d-amphetamine. On the ninth day, all animals received saline injections and were tested in the presence of or in the absence of a novel stimulus. Reaction to the novel stimulus varied inversely with the dose of d-amphetamine which had been received during the drug administration period. This reduction in reaction to the novel stimulus did not seem to depend on the level of amphetamine induced stereotypy at the end of the drug administration period or on general reduction of activity or on interference by drug conditioned responses. 14 references. (Author abstract)

002533 Schuster, Charles R. Pritzker School of Medicine, University of Chicago, Chicago, IL **Project Summary: Psychopharmacology of drug abuse.** Final report, NIMH Grant MH-11052, October 1976.

An animal model of drug dependence based upon the principles of operant conditioning was developed in order to evaluate the abuse potential of drugs. Rhesus monkeys were equipped with intravenous catheters for self-administering a variety of drugs using various procedures including substitution, unlimited access, choice and escape. Using these procedures with diethylpropion and perphenazine, it was shown that animals self-administer the same drugs and in a manner similar to human abuse. Procedures such as choice indicate that diethylpropion has a lower reinforcing efficacy than

cocaine. This corresponds to the reported relative incidence of their abuse. Perphenazine not only was not self-administered in the substitution paradigm, but in addition was escaped. This also corresponds to the relative lack of abuse of the phenothiazines. It is concluded that these procedures are useful for predicting the relative abuse potential of unknown drugs.

002534 Sears, Ronald Joseph. De Paul University **Resistance to punishment and extinction following responding under methamphetamine or secobarbital. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-23713 HC$15.00 MF$8.50 120 p.

Three experiments evaluated the effect of pairing methamphetamine or secobarbital with asymptotic responding in a runway on later undrugged resistance to punishment and extinction in 151 rats. Results indicated that rats which respond under the influence of either 1.0mg/kg methamphetamine or 5.0mg/kg secobarbital in training later showed persistence during punishment or extinction testing in an undrugged state. Results were not due to: 1) presumed aversiveness of the injection procedure; 2) carryover or contrast effects from drug treatment to testing; or 3) specific pharmacological properties or methamphetamine or secobarbital or drug induced response disruption in training. Two alternate explanations were offered. The first was based on a specially developed theoretical position which predicted that treatment with a stimulant drug would result in later persistance, and that treatment with a depressant would lead to later sensitization. Evidence from rat responses supported these predictions. The second view stated that both drugs were aversive (sickness inducing) and that Ss generalized from one aversive stimulus (drug induced sickness) to another (punishment or nonreward). The results also supported this explanation. Recommendations were made for further study to discriminate between the two interpretations. (Journal abstract modified)

002535 Segal, David S. Department of Psychiatry, School of Medicine, University of California at San Diego, La Jolla, CA 92093 **Differential effects of para-chlorophenylalanine on amphetamine-induced locomotion and stereotypy.** Brain Research (Amsterdam). 116(2):267-276, 1976.

The effects of p-chlorophenylalanine (PCPA) on amphetamine induced locomotion and stereotypy were studied in adult male Wister rats weighing 325-375gm. The animals were given either PCPA or vehicle s.c.,followed 48 hr later by amphetamine s.c. In addition, biosynthesis of dopamine was measured in the caudate and putamen following administration of saline, PCPA, amphetamine, or PCPA + amphetamine. In this procedure, synaptosomes were isolated and the conversion of C14-tyrosine to dopamine was measured by the evolution of C14 labeled carbon dioxide. PCPA was found to enhance spontaneous activity 48 hr after injection and potentiated the number of crossovers and rearings induced by amphetamine during the 4 hr period following amphetamine administration. Locomotor activity displaced the characteristic stereotypy seen following large doses of amphetamine. These differential effects of PCPA on amphetamine induced locomotion and stereotypy are in contrast to the uniform pattern of behavioral augmentation resulting from repeated amphetamine administration. Dopamine biosynthesis was reduced to 40% of the control level 2 hr following amphetamine injection. PCPA did not affect dopamine biosynthesis and did not alter the suppression produced by amphetamine. 43 references.

002536 Shibuya, Ken; Nishimori, Tsukao; Matsuda, Kozo; Hayashi, Masaro; Ukida, Tsuneo. Tokyo Medical College, Tokyo, Japan **A pharmacological investigation into the central nervous action of prazepam.** Journal of the Tokyo Medical College (Tokyo). 34(6):1052, 1976.

At the 97th Tokyo Medical College General Symposium for University Medicine held in June 1976 at the Tokyo Medical College, behavior studies were conducted on rats and rabbits to test the central nervous system effects of prazepam (PZP). Naive behavior and conditioned avoidance behavior, as well as brain catecholamine levels, were observed. Dosage of 100mg/kg of PZP in naive behavior conditions produced a muscle relaxing effect, and condition avoidance behavior was effected by doses of 10mg/kg (for single rats) and at 5mg/kg (for rats acting in a group). Brain catecholamine metabolism was inhibited by alpha-methyl-para-tyrosine with dopamine turnover inhibition going in order (greater to smaller) from triazolam, to diazepam, to chlordiazepoxide, to PZP.

002537 Shinoda, Akira; Kawashima, Seiichiro. Gakushuin University, Tokyo, Japan **The effects of androgen on wheel-spinning activity in infant rats.** Annual of Animal Psychology (Tokyo). 26(1):50, 1976.

In a paper read to the 36th Symposium of Japanese Animal Psychologists held in June 1976 at Osaka University, an experiment was done with castrated male infant rats (1 to 5, 6 to 10, and 21 to 25-days-old) by giving some groups androgen (TP) and observing its effects on wheel spinning activity after they had matured. Some were given TP (100mg/day) for a week, and others were later given estrogen (EB, 6.6mg/day) for the same period. Wheel spinning activity was not changed in the TP group, while EB injections increased the activity. Those rats which had received early doses of TP were less receptive to the effects of the EB. The same experiment was performed with rats castrated after maturity, followed by placing an ovary inside them and injecting progestin; the same results were obtained.

002538 Shintomi, Keiichi; Yamamura, Michio; Ishida, Ryuichi. Safety Research Laboratory, Tanabe Seiyaku Co., Ltd., Osaka 532, Japan **Effects of penfluridol and other drugs on methamphetamine-induced stereotyped behavior in monkeys.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):35P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study of the effects of various neuroleptic drugs on methamphetamine induced stereotyped behavior (MA-SB) in male cynomolgus monkeys was reported. Methamphetamine produced a dose dependent stereotyped behavior characterized by continuous licking and biting, and repetitive movement of the hands, head, and body similar to that caused by apomorphine. The severe stereotyped behavior induced by methamphetamine lasted for 8 to 10 hr.,and disappeared after 24 hr. Penfluridol and haloperidol showed definite antagonistic effects on the MA-SB, and chlorpromazine showed a moderate antagonistic effect on the MA-SB. Alpha-methyl-p-tyrosine completely prevented the MA-SB. Reserpine did not inhibit the MA-SB though the drug elicited markedly behavioral depression in monkeys. It is suggested that protection against the MA-SB may be useful for evaluation of neuroleptic drugs in monkeys, and that the MA-SB may be mediated by the dopaminergic mechanism in the extrapyramidal system of monkeys. It is also suggested that studies on stereotyped behavior in monkeys may provide a better understanding of the mechanism of action by which stimulant drugs elicit schizophreniform symptoms in humans. (Author abstract modified)

002539 Shoji, Thoru; Sakurada, Shinobu; Kisara, Kensuke. Department of Chemical Pharmacology, Tohoku College of Pharmacy, Sendai 983, Japan **Increase in spontaneous motor activity of intracerebrally administered metaraminol in mice.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):37P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study of the increase in spontaneous motor activity (SMA) of mice after intracerebral injections of metaraminol (MA) was reported. SMA increased 30 min after MA injection and returned to control levels at 90 min. MA produced a significant decrease of brain dopamine, noradenaline and serotonin 30 min after injection. When MA was injected in isocarboxazide (Iso) pretreated mice, SMA markedly increased as compared with mice receiving either substance alone. When MA was injected in alpha-methyl-p-tyrosine (alpha-MT) pretreated mice, SMA significantly increased as compared with mice receiving alpha-MT alone but SMA did not increase as much as in MA treated animals. In alpha-MT treated mice, L-DOPA restored the hypermotor activity of MA. Diethyldithiocarbamate did not influence the hypermotor activity induced by MA. Haloperidol markedly blocked the hypermotor activity induced by MA. The results support the hypothesis that the central dopaminergic system rather than noradrenergic system plays a leading role in the hypermotor activity induced by MA. (Author abstract modified)

002540 Siegel, R. K.; Brewster, J. M.; Johnson, C. A.; Jarvik, M. E. Department of Pharmacology, University of California, Los Angeles, CA 90024 **The effects of hallucinogens on blind monkeys.** International Pharmacopsychiatry (Basel). 11(3):150-156, 1976.

To investigate reactions to visual stimuli induced by drugs, two blind monkeys were studied with an observational profile that was previously shown to distinguish the effects of hallucinogens from those of other classes of drugs. Observation of the animal for the frequency of 18 behavioral categories showed that lysergic acid diethylamide (LSD) and dimethyltryptamine could be distinguished from saline, chlorpromazine, d-amphetamine sulfate, and bromo-lysergic acid diethylamide by the increased frequency of spasms, stereotypy, bump, and tracking. The hallucinogens also produced dramatic increases in exploration and related behaviors normally seen only in response to real visual or auditory stimuli. It is suggested that the results can be compared to those obtained with sighted monkeys where hallucinogens increased the frequency of spasms and stereotypy, especially in dark environments. It is posited that the type of exploration, tracking, and groping behavior found in the present study constitutes a motor attempt by the animal to verify perceptions. 24 references. (Author abstract modified)

002541 Smee, Martin L.; Overstreet, David H. School of Biological Sciences, Flinders Univ. of So. Australia, Bedford Park, So. Australia 5042, Australia **Alterations in the effects of dopamine agonists and antagonists on general activity in rats following chronic morphine treatment.** Psychopharmacology (Berlin). 49(2):125-130, 1976.

The effects of chronic morphine treatment on general activity induced by dextroamphetamine, apomorphine, haloperidol and pimozide was studied in rats. Morphine alone produced depression of general activity 30 min after a single injection; after 150 min, hyperactivity was observed. Tolerance to the depressive effects of morphine occurred within 7 days of chronic, once daily administration. The depression was replaced by a hyperactivity that included a high degree of self-directed oral stereotyped behavior. Chronic morphine treatments produced supersensitivity to dextroamphetamine, an indirectly acting dopamine agonist, and to apomorphine, a directly acting dopamine agonist. Chronic morphine treatments produced subsensitivity to pimozide, a directly acting dopamine antagonist, and no change in sensitivity to haloperidol, another dopamine antagonist. These findings are consistent with the hypothesis that an increase in the number of dopamine receptors may develop during chronic treatment with morphine. 26 references. (Author abstract modified)

002542 Smith, Donald F. Psychopharmacology Research Unit, Psychiatric Hospital, Risskov, Denmark **Effects of tranylcypromine stereoisomers, clorgyline and deprenyl on open field activity during long term lithium administration in rats.** Psychopharmacology (Berlin). 50(1):81-84, 1976.

Locomotor activity of male rats was studied in an open-field after an intraperitoneal injection (15mg/kg) of the d-isomer or l-isomer of tranylcypromine (d-Tc and l-Tc, respectively) or after subcutaneous injection of either clorgyline (0.5, 1, or 5mg/kg) which selectively inhibits Type A monoamine oxidase (MAO) or deprenyl (0.5, 5 or 10mg/kg) which selectively inhibits Type B MAO. The rats were fed a diet containing either no lithium (control group) or lithium chloride (lithium group) for at least 28 days prior to tests. In the control group, d-Tc increased ambulation, while l-Tc, deprenyl, and clorgyline failed to affect activity. In the lithium group, d-Tc and deprenyl increased ambulation, l-Tc increased ambulation and rearing, while clorgyline failed to affect activity. Lithium appeared to potentiate the behavioral effects of deprenyl and l-Tc. Symptoms of serotonin dependent hyperactivity appeared in the control group and lithium group given d-Tc. The role of biogenic amines in the effects of the drugs on open-field activity is discussed. 25 references. (Author abstract)

002543 Smith, Stanley G.; Werner, Toreen E.; Davis, W. Marvin. Department of Pharmacology, School of Pharmacy, University of Mississippi, University, MS 38677 **Effect of unit dose and route of administration on self-administration of morphine.** Psychopharmacology (Berlin). 50(1):103-105, 1976.

In a study of the effect of unit dose and route of administration on the self-administration of morphine, rats were implanted with intravenous or intragastric cannulas and allowed to self-administer morphine sulfate in doses of 0 (saline), 0.03, 0.1, 0.3, 1.0, 3.0, and 10.0mg/kg/infusion. For the intravenous route the number of infusions decreased with increasing unit dose, while the amount self-administered was directly related to unit dose. However, for the intragastric route the number of infusions first increased and then decreased as unit dose was elevated, while the amount self-administered again increased with unit dose. Comparisons between routes showed that for intragastric subjects the number of infusions and amount self-administered both were lower at the two lowest doses but higher for all other doses. These results support the expectation that intravenous injection should produce more potent reinforcing effects than intragastric administration. 7 references. (Author abstract modified)

002544 Soubrie, P.; De Angelis, L.; Simon, P.; Boissier, J. R. Unite de Recherche de Neuropsychopharmacologie de l'I.N.S.E.R.M. 2, Rue d'Alesia, F-75014 Paris, France /**Effects of antianxiety drugs on the water intake in trained and untrained rats and mice.**/ Effets des anxiolytiques sur la prise de boisson en situation nouvelle et familiere. Psychopharmacology (Berlin). 50(1):41-45, 1976.

The effects of antianxiety agents on water intake were studied in trained and untrained rats and mice. Water deprived animals trained to the test situation spent more time in drinking than naive animals (first exposure to the test situation). The time spent in drinking, either during 5 min or during 10 min, was recorded. As compared to controls, benzodiazepines, phenobarbital, meprobamate, and methoqualone increased drinking time whether the experiments were run on naive or on experienced animals. This release of the drinking behavior was more pronounced during the last 5 min of the 10 min test session. These results suggest that the inhibition of water intake of naive animals as compared to trained rats and mice could be related to some emotional factors elicited by the first exposure to an unknown situation. It is suggested that the increase in drinking time induced by the antianxiety drugs in a novel and in a familiar situation seems difficult to correlate only with the antianxiety action of these compounds. It is concluded that antianxiety drugs could interfere with the regulator mechanism of thirst. 13 references. (Author abstract modified)

002545 Tagashira, Eijrio; Izumi, Tomoko; Yanaura, Saizo. Department of Pharmacology, Hoshi College of Pharmacy, Tokyo 142, Japan **Studies on drug dependence (Rept. 19): dependence on preference on and preference for morphine.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):43P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study of choice behavior for morphine (M) or codeine (C) admixed diets in rats injected with M or C was reported. M dependent rats subcutaneously injected with gradually increased doses showed a lower intake ratio as compared to M dependent rats which ingested M admixed diet, despite a larger M administration. This relationship was also demonstrated in C dependent rats. Decrease in body weight was 12.0% in the former while no body weight loss was observed in the latter. Rats receiving injections of M in combination with the M admixed diet showed a more intensive choice behavior for M than those receiving M injection alone. In cross-spontaneous M intake behavior between M and in C dependent rats, rats injected with C ingested 20% M admixed diet under M admixed vs. normal diet situations, and body weight decreased 9.0% after the first 48 hr. It is suggested that M injected rats acquire almost the same degree of physical dependence as compared to rats ingesting the M admixed diet. Rats treated with the M admixed diet proved to be the most sensitive animals as models of M seeking behavior under choice conditions. (Author abstract modified)

002546 Takada, Kohji; Ando, Kiyoshi; Yanagita, Tomoji. Department of psychopharmacology, Central Institute for Experimental Animals, Kawasaki 211, Japan **Operant behavioral observation on visual and auditory effects of drugs.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):105P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March 1976, a study of the visual and auditory effects of quinidine lysergic acid diethylamide-25 (LSD-25) and pilocarpine on rats and rhesus monkeys was reported. Rats and rhesus monkeys were trained to press a lever for food reinforcement. Lever pressing during the auditory and visual stimulus periods was punished by electric shock. Complete suppression of the responses in the stimulus period and stable responses in the stimulus free period were observed. The auditory threshold of rats and the visual threshold of monkeys were determined by the discrete tracking method. The stimulus intensity was decreased or increased by a fixed degree, according to the suppression rate of the responses in the stimulus period. Quinidine elevated the auditory threshold of rats, while the response suppression in the visual stimulus period and the responding rate in the stimulus free period were not affected. LSD-25 markedly elevated the visual threshold of one monkey. The threshold of another monkey was not affected although the rate of response decreased. Pilocarpine applied to a monkey's eyeball constricted the pupil and elevated the visual threshold. It was concluded that the drugs tested had specific effects on the sensory functions of the animals, and that this method can be of use for assessing the toxic effects of chemical substances on auditory and visual sensations. (Author abstract modified)

002547 Takeuchi, Koji; Okabe, Susumu; Takagi, Keijiro Faculty of Pharmaceutical Sciences, University of Tokyo, Bunkyo-ku, Tokyo 113, Japan **Influence of amylopectine sulfate on gastric mucosa in normal or water-immersion stressed rats.** Japanese Journal of Pharmacology (Kyoto). 26(4):506-509, 1976.

An investigation was carried out to determine: 1) whether amylopectine sulfate (APS) induces damage to the stomach of rats in normal conditions; 2) whether APS influences stress ulcers developed in rats with an intact pylorus; and 3) the effects of various pharmacological agents on APS induced gastric ulcers. APS significantly inhibited the formation of ulcers induced by water immersion stress in rats without pylorus ligation. However, APS strongly irritated the gastric mucosa of normal rats and stressed rats with pylorus ligation. The degree of gastric damage induced by APS was far greater in stressed rats than in normal rats. Concomitant administration of sodium bicarbonate, atropine sulfate or L-glutamine with APS prior to stressing potently inhibited APS induced gastric damage. The mechanisms by which APS produces gastric damage under stressful situations is discussed. 20 references.

002548 Valdman, A. V.; Zvartau, E. E.; Kozlovskaya, M. M. Department of Pharmacology, Pavlov Medical Institute, Leningrad, P-98, 197089, USSR **Experimental study of the action of psychotropic drugs on emotions, motivations and social behavior of animals.** In: Airaksinen, M., CNS and behavioural pharmacology. Elmsford, New York, Pergamon Press, 1976. 344 p. v. 3. (p. 207-211).

In a paper presented at the Sixth International Congress of Pharmacology held in Helsinki, Finland in July, 1975, objective criteria for assessing the emotional state of an animal and the behavioral criteria which reveal the individual psychotropic spectrum of a drug being evaluated are discussed. It is suggested that such criteria are changes in the reactions of an animal to environmental (especially social) stimuli under the conditions of normal emotional state and an emotional state modified by central electrical stimulation and changes in operant behavior in an animal controlled by central electrical stimulation. Studies are reported in which cats were placed in a group, their reactivity to the environment and to the other animals noted, and the effects of drugs on shifts in their emotional state produced by electrical stimulation of the emotiogenic areas of the brain were assessed. Chlordiazepoxide increased pleasure reactions and suppressed punishment effects. Diazepam strongly inhibited diffuse alarm, neurotic stress, and fear. Oxazepam evoked an increase in initiative. Nitrazepam suppressed the orienting response and evoked early neurotoxic symptoms such as ataxia. It is suggested that the effect of drugs strongly depends upon both the type of drug and the individual characteristics of the animal and that this complex behavioral approach allows the individual spectra

of drug action to be revealed. In other studies, the effects of haloperidol, chlordiazepoxide, and pentobarbital on negative effects and positive effects of central electrical stimulation, as assessed by escape from an area of a shuttle box in which stimulation is activated to an area in which stimulation is not activated, or by lack of escape, respectively, were studied. Ambivalent effects may also be assessed by return responses in this procedure. Haloperidol did not affect the escape response but decreased returns to the active part of the box. Chlordiazepoxide facilitated the escape reaction and strongly stimulated the return response. Pentobarbital suppressed escape responses but facilitated return responses. It is suggested that the data indicate that chlordiazepoxide does not affect the perception of an aversive stimulus but inhibits the emotional reaction to it, while pentobarbital inhibits both perception of and emotional reactivity to an aversive stimulus.

002549 Vogel, John R.; Nathan, Beth A. Bristol Laboratories, Box 657, Syracuse, NY **Reduction of learned taste aversions by pre-exposure to drugs.** Psychopharmacology (Berlin). 49(2):167-172, 1976.

The effect of prior exposure to psychotropic drugs on the development of tolerance to drug induced taste aversions was studied in rats. Taste aversions induced by amobarbital were reduced by prior exposure to the drug. Increasing numbers of preexposures were associated with larger reductions in taste aversions. Reductions in sleeping time, an accepted measure of tolerance to barbiturate drugs, were not correlated with reductions in taste aversions. Taste aversions induced by amobarbital were also impaired following preexposure to the pharmacologically dissimilar drug dextroamphetamine. It is suggested that reduced taste aversions following preexposure to drugs may reflect habituation to drug related stimuli and not solely the development of tolerance to the drugs. 22 references. (Author abstract modified)

002550 Vogel, Richard Allan. Johns Hopkins University, Baltimore, MD 21218 **Effects of carbon monoxide, hypoxic hypoxia, and drugs on animal models of complex learned behavior. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-22958 HC$15.00 MF$8.50 191 p.

The effects of hypoxic hypoxia, carbon monoxide, and three prototypical psychotropic drugs on animal models of complex learned behavior were studied and several new discrimination tasks were developed using pigeons and baboons as Ss. Five pigeons were trained to perform a discrimination task allowing variability of reinforced response patterning. Three baboons were trained to move a yellow light within a matrix of light positions until it was superimposed on a blue light by manipulating a four directional level. Results were in accordance with previous data that variability of patterns of responding decreases with practice, and that the degree of stimulus control determines the sensitivity of performance to disruption. With the complex baboon paradigm, comparison of the drug effects revealed heretofore unobserved differences between the three compounds that were not related to their motivational effects. The development of this new paradigm suggested that in order to distinguish behavioral effects of psychotropic drugs, rate and accuracy measures may not be sufficient, but changes in response pattern profiles may be necessary as well. This paradigm is seen as clearly providing this type of analysis. (Journal abstract modified)

002551 Wahlstrom, Goran. Department of Pharmacology, University of Umea, S-90187 Umea, Sweden **The interaction between pilocarpine and hexobarbital in male rats.** Psychopharmacology (Berlin). 49(2):159-166, 1976.

The effect of pilocarpine on the dose of hexobarbital required to produce an EEG criterion (the silent second) was studied in rats. Pilocarpine in doses of 25mg/kg to 50mg/kg administered 1 h prior to hexobarbital increased the amount of hexobarbital required to obtain this criterion. With higher doses of pilocarpine, increases in hexobarbital thresholds occurred if no convulsion was induced by pilocarpine. If a convulsion occurred, the dose of hexobarbital was reduced. Similar results were obtained in studies in which pilocarpine was administered at different times prior to the hexobarbital. Convulsions were more likely to occur when the interval between pilocarpine administration and hexobarbital administration was increased. In animals without convulsions the effect of pilocarpine on the dose of hexobarbital was counteracted by atropine. The acute effects of pilocarpine on the hexobarbital threshold mimic the events which occur during the abstinence after chronic barbiturate treatments. It is suggested that pilocarpine and perhaps other cholinergic agonists could be regarded as model substances for tolerance and abstinence seen after chronic barbiturate treatments. 27 references. (Author abstract modified)

002552 Watson, P. J.; Cox, Verne C. Psychology Department, University of Texas at Arlington, Arlington, TX 76019 **An analysis of barbiturate-induced eating and drinking in the rat.** Physiological Psychology. 4(3):325-332, 1976.

A threefold study was undertaken: 1) to explore the motivational effects of pentobarbital and phenobarbital on eating and drinking in the rat; 2) to present evidence relevant to possible explanations of the drug action; and 3) to determine if there is a relationship between barbiturate induced behaviors and electrical stimulation of the lateral hypothalamus. Results indicate systemic injections of pentobarbital and phenobarbital induced nondeprived animals to eat and to drink. The feeding was not secondary to osmotic changes brought on by drinking, and the drinking was not dependent upon eating. Responses to pentobarbital were quantitatively and qualitatively different from behaviors elicited by lateral hypothalamic stimulation. 27 references. (Author abstract modified)

002553 Weiner, William J.; Kanapa, Dorothy J.; Klawans, Harold L. Division of Neurology, Michael Reese Hospital and Medical Center, Chicago, II 60616 **The effect of dimethylaminoethanol (deanol) on amphetamine- induced stereotyped behavior (AISB).** Life Sciences (Oxford). 19(9):1371-1375, 1976.

The effect of dimethylaminoethanol (deanol) on amphetamine induced stereotyped behavior (AISB) in guinea-pigs was studied. Deanol had no effect on AISB which suggests that deanol has little if any central cholinergic effect on dopamine related stereotyped behavior. This lack of central cholinergic effect is discussed in relationship to the reported clinical efficacy of deanol in human movement disorders. 32 references. (Author abstract)

002554 Weston, P. F.; Overstreet, D. H. Biological Sciences, Flinders University of South Australia, Bedford Park, South Australia, 5042 **Does tolerance develop to low doses of d- and l-amphetamine on locomotor activity in rats?** Pharmacology Biochemistry and Behavior. 5(6):645-649, 1976.

An observational study of the behavioral effects of chronic regimens of d- and l-amphetamine was designed to investigate possible mechanisms underlying any parallel behavioral

changes: 1) accumulation of p-hydroxynorephedrine in noradrenergic nerve terminals; 2) altered sensitivity of dopaminergic receptors. The study revealed that locomotor activity seen with low doses of both isomers (2.0mg/kg d- and 6.0mg/kg l-) decreased with chronic once daily treatments. However, this was accompanied by an increase in directed sniffing activity and the behavior came to resemble that seen with higher doses of amphetamine (8.0mg/kg d- and 16.0mg/kg l-). Nonsignificant decreases in locomotor activity and increases in directed sniffing to apomorphine administration were observed during chronic amphetamine treatment. These findings suggest that p-hydroxynorephedrine, a metabolite of d-amphetamine but not l-amphetamine, does not play an important role in these alterations in behavior with chronic treatment, and the tolerance to amphetamine observed under these conditions is due to an increased, rather than decreased, sensitivity of the rats to amphetamine. 23 references. (Author abstract)

002555 Will, Bruno; Maurissen, Jacques; Ropartz, Philippe; Kempf, Eliane; Mack, Gerard; Mandel, Paul. Laboratoire de Psychophysiologie, Universite Louis Pasteur, 7, rue de l'Universite, F-67000 Strasbourg, France **Catecholamines and operant response rates in albino rats.** Psychopharmacology Communications. 2(3):219-229, 1976.

Catecholamine effect on the operant response rates in rats was studied. The action of d-amphetamine was studied in rats conditioned on an operant multiple schedule of reinforcement. The action of this drug depended on the control response rate of each individual. The turnover of brain norepinephrine (NE) and dopamine (DA) was estimated in the whole brain of the same rats; the steady state level of NE, but not the turnover time, was significantly correlated with the average response rate of each subject. No significant correlation was found between this response rate and the turnover of DA. It is proposed that the response rate dependent effects of d-amphetamine might be related to brain NE levels. 21 references. (Author abstract)

002556 Wilson, M. C.; Bedford, J. A.; Buelke, J.; Kibbe, A. H. School of Pharmacy, University of Mississippi, University, MS 38677 **Acute pharmacological activity of intravenous cocaine in the rhesus monkey.** Psychopharmacology Communications. 2(3):251-261, 1976.

The effects of the intravenous administration of cocaine on body temperature, heartrate, respiration rate, and several unconditioned behavioral categories were ascertained in unanesthetized male rhesus monkeys. Statistically significant increases in body temperature, respiration rate and heartrate occurred only after the largest dosage tested. Subjective increases in pupil size, activity, reactivity, and vocalization as well as the occurrence of stereotyped behaviors, mydriasis, and refusal to ingest fruit were observed following injection. A large degree of consistent intersubject variability in the magnitude of these responses was present. There was no consistent correlation across subjects between the magnitude of these responses and the plasma level of cocaine. However, within a given subject a direct correlation existed between these parameters. 9 references. (Author abstract)

002557 Wolfarth, S.; Vetulani, J.; Dulska, E.; Golembiowska-Nikitin, K. Institute of Pharmacology, Polish Academy of Sciences, 12 Smetna Str., 31-344 Krakow, Poland, **Cholinergic-dopaminergic interactions at the level of substantia nigra in the rabbit.** Naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 294(Supplement):63, 1976.

In a paper presented at a pharmacology meeting in Hannover, Germany, on September 14-17, 1976, cholinergic/dopaminergic interactions at the level of substantia nigra in the rabbit were described. Unilateral intranigral injections of apomorphine (APO) depressed locomotor activity and increased relaxed EEG patterns in the rabbit, while carbachol (CCh) increased the locomotor activity, elevated the alert index, and produced episodes of epileptoid discharges, usually beginning in substantia nigra. It is concluded that APO and CCh exert mutually antagonistic effects at the level of substantia nigra, but that they control the striatal dopaminergic mechanisms acting through different pathways. (Author abstract modified)

002558 Yanagita, Tomoji. Central Institute for Experimental Animals, Kawasaki 211, Japan **Nicotine and behavior.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):25P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a review of the operant behavioral effects of nicotine (N) and the role of N as a reinforcer of an animal's N taking behavior was presented. N has diverse effects of facilitation and suppression on various types of behavior such as conditioned avoidance, discriminated avoidance, and Sidman avoidance responses. Wide individual and strain differences exist in the susceptibility to the behavioral effects of N. N suppresses such behavior when large doses are given. The facilitative or suppressant effect tends to be demonstrated when the baseline rate is low or high, respectively. From these data it is assumed that both central and peripheral mechanisms are involved in the behavioral effects. N induced reinforcement of animals' drug seeking and taking behavior has been observed both in rhesus monkeys and rats. In monkeys, N was self-administered regularly at stable dose levels by each monkey only in the daytime without any marked toxic behavioral manifestations. In rats, however, the intake was very erratic and at active phases they usually manifested such toxic symptoms as tremor, convulsions and even acute death. It is concluded that cigarette smoking is a type of conflicting behavior, and its development is a matter of balancing the rewarding pharmacological effects with such punishing effects as overdose pharmacological effects and local irritative effects of the smoke on the animals' respiratory organs. (Author abstract modified)

002559 Young, Gerald A.; Moreton, J. Edward; Khazan, Naim. Department of Pharmacology and Toxicology, University of Maryland School of Pharmacy, Baltimore, MD 21201 **Duration of action of naloxone subcutaneous pellets in antagonizing the eeg and operant behavioural effects of morphine in the rat.** Journal of Pharmacy and Pharmacology (London). 28(8):658-660, 1976.

The duration of action of the pellet depot formulation of naloxone in antagonizing the EEG and operant behavioral effects of morphine in postaddicted rats is investigated. It was demonstrated that the naloxone subcutaneous pellets that effectively prevented relapse to morphine self-administration blocked both the REM sleep suppressant effects and the operant behavior suppressant effects of morphine for approximately 2 weeks. It is suggested that the two experimental models used in the present study to assess the duration of action of naloxone pellets in antagonizing morphine effects may contribute to the delineation of duration of action of long-acting preparations of morphine antagonists. 14 references.

002560 Zalewski, Casimir John. Wayne State University, Detroit, MI 48202 **Correlation of behavioral, biochemical, and**

locomotor effects of select psychotropic agents in the mouse. (Ph.D. dissertation). Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-26196 HC$15.00 MF$8.50 225 p.

Chlordiazepoxide HCL (CDP), chlorpromazine HCL (CPZ), amobarbital sodium (AMO), and dextroamphetamine sulfate (DAS) were investigated for their behavioral, biochemical, and locomotor effects in the mouse. General trends of the four psychotropic compounds on conditioned behavior and locomotor activity mean latencies, mean avoidances, and brain amine levels showed similarities and differences in their behavioral and biochemical levels. Conditioned behavior mean latencies were primarily decreased with CDP and AMO doses and increased with CPX and DAS doses. Mean avoidances were overall increased with CDP and AMO doses, while locomotor activity mean latencies were generally increased with doses of each compound. CDP doses increased norepinephrine, dopamine and 5-hydroxytryptamine levels at 15 min and 60 min periods and to a lesser degree at a 30 min period. (Journal abstract modified)

002561 Zebrowska-Lupina, I.; Przegalinski, E.; Sloniec, M.; Kleinrok, Z. Department of Pharmacology, School of Medicine, Jaczewskiego 8, 20-090 Lublin, Poland **Clonidine-induced locomotor hyperactivity in rats.** naunyn-Schmiedebergs Archives of Pharmacology (Berlin). 294(Supplement):R14, 1976.

In a paper presented at a pharmacology meeting in Hannover, Germany, September 14-17, 1976, the effect of clonidine on locomotor activity of rats in experimental conditions allowing to eliminate presynaptic noradrenaline (NA) receptor activation in the brain was reported. In some experiments the action of clonidine was also observed after alpha-methoxytryptamine (alpha-MT) and parachlorophenylalanine (PCPA) in rats pretreated with 6-hydroxydopamine (6-OHDA). Clonidine produced locomotor hyperactivity in rats pretreated with 6-OHDA plus reserpine; 6-OHDA plus alpha-MT plus PCPA; and reserpine plus a low dose of yohimbine. It was concluded that in experimental conditions allowing selective activation of central postsynaptic NA receptors, clonidine can induce hyperactivity instead of sedation. (Author abstract modified)

05 TOXICOLOGY AND SIDE EFFECTS

002562 Baum, Thomas; Peters, John R.; Butz, Frank; Much, David R. Cardiovascular Pharmacology Section, Wyeth Laboratories, Inc., Radnor, PA 19087 **Tricyclic antidepressants and cardiac conduction: changes in ventricular automaticity.** European Journal of Pharmacology (Amsterdam). 39(2):323-329, 1976.

An examination of the influence of tricyclic antidepressants on ventricular automaticity is reported. It is pointed out that ventricular dysrhythmias result from changes in the automaticity of the conduction properties of the specialized conduction system and tricyclic antidepressants have been reported to cause ventricular dysrhythmias in humans and experimental animals. Ventricular rhythm was produced in anesthetized dogs by blocking atrioventricular conduction. Low doses of imipramine, amitriptyline and nortriptyline resulted in small but significant increases in automaticity. Relatively high doses of these agents suppressed automaticity markedly. It is concluded that these changes could play a role in the development of dysrhythmias. 28 references. (Author abstract modified)

002563 Creel, Donnell; Shearer, Donald E.; Hall, Peter F. Neuropsychology Research, 151-A, Veterans Administration Hospital, Salt Lake City, UT 84148 **Differences in cytochrome P-450 of various strains of rats following chronic administration of pentobarbital.** Pharmacology Biochemistry and Behavior. 5(6):705-707, 1976.

To determine if differences exist in levels of hepatic cytochrome P-450 between several albino and pigmented strains of rats following progressively increasing doses of pentobarbital sodium and physiological saline, cytochrome P-450 levels were analyzed in rats of two pigmented (black Long-Evans and ACI) and two albino strains (Fischer 344 and Sprague-Dawley). Differences between the albino vs pigmented strains were observed following injections of saline. The Fischer 344 albino strains responded similarly to the pigmented strains following a progressively increasing dose schedule of pentobarbital sodium. 20 references. (Author abstract)

002564 Fujii, Takaaki. Safety Assessment Laboratories, Nippon Merck-Banyu Co., Ltd., Okazaki, Aichi 444, Japan **Mitigation of caffeine-induced fetopathy in mice by pretreatment with beta-adrenergic blocking agents.** Japanese Journal of Pharmacology (Kyoto). 26(6):751-756, 1976.

The relation between time intervals of propranolol pretreatment and its effect on reducing caffeine induced fetopathy in mice was investigated, and the fetopathy reducing effect of timolol was compared with that of propranolol. Propranolol (5mg/kg) administered 15, 30, or 60 minutes before caffeine treatment significantly reduced the caffeine induced fetopathy. The optimal effect was found when propranolol was given 30 minutes before caffeine. The reduction in fetopathy by timolol pretreatment was comparable to that of propranolol. The results lend support to the hypothesis that the fetopathic effect of caffeine is linked with released catecholamines in maternal or fetal tissues of mice. 18 references. (Author abstract modified)

002565 Fujimori, Kannosuke; Nagao, Shigeyuki; Omori, Yoshihito; Kaneko, Toyozo; Horiuchi, Shigetomo. Department of Toxicology, National Institute of Hygienic Sciences, Tokyo 158, Japan **Effect of chronic treatment of methylmercuric chloride on the central nervous system in rats.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):83P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March 1976, a study of the mechanism by which methylmercury chloride (MMC) produces its neurotoxic effects in rats was reported. After 4 weeks of MMC in the diet a reduction of motor coordination associated with a slight motor functional impairment of the hind limb was observed in testing on the rotarod. After 5 weeks, a reduction in norepinephrine (NE) in the midbrain, cerebellum, and medulla/pons was observed but the decreases were not statistically significant. After 7 weeks, the animals could not remain on the rotarod and conditioned avoidance responding was lower than that of controls. After 9 weeks, the grasp holding time was markedly decreased. In the 10th week, the concentrations of NE were decreased in all regions and the decreases in midbrain, cerebellum, and medulla/pons were significant. A significant increase in dopamine was measured in the cortex only. The conductance velocity of the hind limb nerve was markedly reduced after long term MMC. It is suggested that the neurotoxic effects of MMC are related to the reduction in brain NE. (Author abstract modified)

002566 Furukawa, Tatsuo; Tokuda, Masatake. Department of Pharmacology, School of Medicine, Fukuoka University, Fukuoka 814, Japan **Effects of rubidium on behavioral responses to methamphetamine and tetrabenazine.** Japanese Journal of Pharmacology (Kyoto). 26(4):395-402, 1976.

The effects of rubidium on spontaneous locomotor activity, methamphetamine induced hyperlocomotor activity and tetrabenzine induced decreases in ambulation, catalepsy, jumping behavior and Straub tail responses were studied in mice. Single doses of rubidium did not affect spontaneous locomotor activity; however, repeated administration tended to increase locomotor activity slightly. Methamphetamine induced locomotor activities were potentiated by rubidium. Monotonic decreases in ambulation after tetrabenzine were not significantly affected by rubidium; however, the decreases were sometimes preceded by slight increases in ambulation and recovery from the decrement tended to be more rapid in rubidium treated animals. Incidences of tetrabenzine induced catalepsy were increased in rubidium treated animals, and jumping behavior and Straub tail responses occurred in a few cases. The results are compared with those of previous studies using lithium. 26 references. (Author abstract modified)

002567 Itoh, Tadanobu; Ando, Fusae; Seki, Mihoko; Nakaya, Shigetsuna. Department of Pharmacology, School of Medicine, Iwate Medical University, Morioka 020, Japan **Effect of chlorpromazine on the reproduction in rats.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):90P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study of the effects of chlorpromazine (CPZ) administration to sexually immature male and female rats (generation I) for 9 weeks before mating on the behavior, bodyweight, and reproduction cycles of generation I, generation II, and generation III was reported. CPZ produced dose related effects in generation I consisting of: 1) inhibition of bodyweight gain; 2) prolongation of the vaginal estrus cycle; 3) decreases in copulation and conception rates; and 4) decreases in the number of live fetuses and corpora lutea on day 14 and day 21 of pregnancy. During the nursing periods, bodyweights of generation II were decreased but those of generation III were increased. Definite prolongation of estrus cycle and decreases in conception rates in generation II were not apparent. (Author abstract modified)

002568 Kazaryan, A. S.; Gizhlaryan, M. S.; Kanayan, A. S. no address **/Toxicity of trichlorobutadiene in subacute experiments./** Toksichnost' trikhlorbutadiena v podostrykh opytakh. Zhurnal eksperimental'noy i klinicheskoy meditsyny (Yrevan). 16(3):26-31, 1976.

Texicity of trichlorbutadiene, used in glue production was tested in 40 white rats including (20 controls) over a period of 65 days. Analsyis of results from inhalation and ingestion of trichlorbutadiene shows the polytropic character of its action, including changes in the central nervous system, with decrease in excitability in the first phase and increase in the second. The central nervous action of chlororganic substances is discussed. 15 references.

002569 Kobayashi, Kazuo; Tobe, Masuo; Suzuki, Sachiko; Kawasaki, Yasushi; Sekita, Kiyoshi; Matsumoto, Kiyoshi. Department of Toxicology, National Institute of Hygienic Sciences, Tokyo 158, Japan **Long-term toxicity study of methylmercuric chloride in monkeys (report V).** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):84P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a neurohistological study of the long term toxicity of methylmercurie chloride in monkeys was reported. In monkeys treated with 0.1mg/kg or 0.3mg/kg of methylmercury per day, the most prominent and exclusive changes were neuronal degeneration and depopulation, appearance of abundant swollen bodied astrocytes, activation of microglia and spongy transformation in the occipital and parietal cortex. In some cases these changes were observed in the temporal and frontal cortex. Cortical changes, if severe, occasionally extended to the subcortical white matter but no changes were evident in the deep white matter. Basal ganglia, diencephalon, midbrain, pons and medulla oblongata were in general not affected. Exceptions were focal lesions in the internal segment of globus pallidus, medial nuclei of thalamus, tegmental region of brainstem and olive in some animals. Cerebellar cortex and white matter were free from changes. No changes were observed in the spinal cord and sciatic nerve. The severity and extent of the changes were more marked in animals fed the higher doses. (Author abstract modified)

002570 Maczynska-Rusiniak, Barbara; Nurowska, Krystyna. Instytut Hematologi, ul. Chocimska 5, 00-791 Warsaw, Poland **/Cytotoxic action of psychotropic drugs on leukocytes in vitro./** Cytotoksyczne dzialanie in vitro lekow psychotropowych na krwinki biale. Psychiatria Polska (Warszawa). 10(3):267-273, 1976.

An in vitro test was made of the action of 31 psychotropic drugs on leukocytes from healthy subjects. It was found that the majority of drugs tested have damaging effect on leukocytes, particularly at higher concentrations. Drugs showing the highest cytotoxic action in vitro were: levopromazine, flufenazine, chlorpromazine, and promazine. Drugs producing no damaging effect are: clozapine, flufenazine decanoate, thiotixene, prochlorpromazine, nialamid, and azafen. 24 references.

002571 Marco, E.; Mao, C. C.; Cheney, D. L.; Revuelta, A.; Costa, E. Laboratory of Preclinical Pharmacology, National Institute of Mental Health, Saint Elizabeths Hospital, Washington, DC 20032 **The effects of antipsychotics on the turnover rate of GABA and acetylcholine in rat brain nuclei.** Nature (London). No. 5584:363-365, 1976.

Experiments with rats show that the action of clozapine, chlorpromazine, and haloperidol on the turnover rates of acetylcholine and GABA in the nucleus caudatus, nucleus accumbens, globus pallidus, and substantia nigra allows for a qualitative differentiation between the biochemical effects elicited by clozapine and cataleptogenic antipsychotics. Results shed light on a possible functional interdependence among GABA, acetylcholine and dopamine in neuronal systems of single brain nuclei, as well as providing some biochemical information which may allow the prediction of a pattern of specific neurotransmitter involvement in the genesis of the cataleptogenic effects of antipsychotics. 26 references.

002572 Pashinskiy, V. G.; Aref'yeva, A. K.; Motovilova, V. G.; Ponomareva, L. V.; Sedova, K. S.; Fil'tsanova, G. A.; Pomanova, T. V. Novokuznetskiy NI khimiko-farmatsevticheskiy institut. Novokuznetsk, USSR **/Experimental study of nozepam toxicity./** Izucheniye toksichnosti preparata nozepama v eksperimente. Farmakologiya i Toksikologiya (Moskva). 39(5):638-640, 1976.

A study was made of the toxicity of nozepam in single and extended injections, compared with the foreign preparation (oxazepam) in experiments with mice, rats, and dogs. Indices

used were morphological study, composition of peripheral blood, and biochemical analysis. Injections for a 3 month period in rats and a 3 week period in dogs produced no toxic organic changes. Chronic toxic effects were the same for both drugs. 4 references.

002573 Przegalinski, E.; Zebrowska-Lupina, I.; Wojcik, A.; Kleinrok, Z. Department of Pharmacology, School of Medicine, Jaczewskiego 8, 20-090 Lublin, Poland **5-Methoxytryptamine-induced head twitches in rats.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 294(Supplement):R14, 1976.

In a paper presented at a pharmacology meeting in Hannover, Germany, September 14-17, 1976, it is reported that in rats pretreated with pargyline, injection of 5-methoxytryptamine (5-MT), produced characteristic head twitches similar to those induced by 5-hydroxytrytophan (5-HTP). 5-HT receptor blocking agents (cyproheptadine, methergoline, mianserine, methysergide, and WA-335-BS) reduced the effect of 5-MT. Antagonism of 5-MT induced head twitches and dissociation between doses effective in this test and those inhibiting the pinna reflex may be of value in the prediction of central 5-HT receptor blocking properties. (Author abstract modified)

002574 Sherman, Arnold D.; Gal, E. Martin. Department of Psychiatry, University of Iowa, 500 Newton Road, Iowa City, IA 52242 **Studies on the metabolism of 5-hydroxytryptamine (serotonin). VII. Effects of haloindoles on cerebral 5-HT in various species.** Psychopharmacology Communications. 2(3):285-293, 1976.

In a comparative study, the effect of intraventricularly or intraperitoneally injected p-chloroamphetamine (p-CA) and some chloroindoles on cerebral levels of serotonin was evaluated. 5-Chloroindole depressed 5-hydroxytryptamine (5-HT) levels in the brainstem and telencephalon for 3 days, but 6-chloro-2-methylindole (6-CMI) only during the first day. 5-Chloroindazole had no effect at all. p-CA was more toxic to guinea pigs than to rats. p-CA and 5-chloro-2-methylindole (5-CMI) had no effect on cerebral 5-HT in chicks. Apparently, none of these compounds represented or was converted to a metabolite possibly responsible for the neurotoxic effects of p-CA. 9 references. (Author abstract)

002575 Shimada, Kiyoko; Hosoya, Eikichi. Department of Pharmacology, School of Medicine, Keio University, Tokyo 160, Japan **Changes in the body weight of rat on continuous injections of morphine, pethidine, or pentazocine.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):42P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study of the changes in body weight of rats after cessation of a 24 hr continuous intravenous infusion of morphine, pethidine, cyclazocine, or pentazocine and after precipitation of withdrawal by naloxone following cessation of an infusion was reported. A gain in body weight was observed only after cessation of pethidine (up to 50mg/kg/24h). After cessation of larger doses of pethidine or after withdrawal of the other drugs (either by cessation or by naloxone), body weight decreases ranging from 1.5% to 8% and persisting from 2 hr to 6 hr were observed.

002576 Smol'yanikova, N. M.; Strekalova, S. N.; Boyko, S. S. Institut farmakologiya AMN SSSR, Moscow, USSR **/Regularities in penetration of the placental barrier by aminazine./** Zakonomernosti pronikaniya aminazina cherez platsentarnyy bar'er. Farmakologiya i Toksikologiya (Moskva). 39(5):560-562, 1976.

A study was made to determine whether aminazine (chlorpromazine) is present in tissues of the newborn when the mother has received injections during pregnancy, and what effect the drug has on embryonic development with injections throughout pregnancy. Rats were given the drug on 7th, 14th, and 21st days, and for 21 days of the cutive pregnancy. Aminazine was found to occur in small quantities in the blood only with a second injection. With repeated injections it occurs in tissue of the liver and brain of newborn rats and in the liver of 1-week-old animals, but the rats do not differ in weight and body measurements from controls. 11 references.

002577 Tollenaere, J. P.; Moereels, H.; Protiva, M. Janssen Pharmaceutica Research Laboratories, B-2340 Beerse, Belgium **Quantitative structure activity relationships (QSAR) in a series of neuroleptic 10-piperazine-dibenzo(b,f)thiepins, ataxia in mice.** European Journal of Medicinal Chemistry (Paris). 11(4):293-298, 1976.

The Automatic Quantitative Structure/Activity Relationships (QSAR) Finder program was used to determine 17 derivatives of 10-piperazino-dibenzo(b, f)thiepins. The rotating rod activity in mice was governed by the electronic character of the substituents, the bulkiness or the effective size of the substituents as expressed by the E(s) constant of R. W. Taft, and a parabolic dependence on the molar volume of the substituents. The optimal molar volume of the substituent was calculated. Results are discussed in terms of the QSARs of other tricyclic neuroleptics. 69 references. (Author abstract modified)

002578 Trzeciak, H. I.; Herman, Z. S.; Szkilnik, R. Department of Pharmacology, Biological-Physiological Institute, Silesian School of Medicine, 41-808 Zabrze, Poland **Behavioral effects of withdrawal of fluphenazine after long-term treatment.** Arzneimittel-Forschung (Aulendorf). 26(9):1697-1700, 1976.

An abstinence syndrome elicited by long-term treatment with fluphenazine is described. Male Wistar rats, 6 wks old, were injected i.p. with 1mg/kg fluphenazine daily except Sunday for 28 wks, or with 5mg/kg for 21 wks. In another series of experiments, 1mg/kg fluphenazine was injected from the 8th day of life into male and female rats born from two females treated during pregnancy and lactation with the same dose of drug. This group of rats received fluphenazine for 32 wks. Control animals in both experiments received saline i.p. The behavior of the rats was observed 48 hr after the last dose, and during the next 4 days, when rats were again treated with the drug. Duration of walking, washing, and immobility was measured in rats during a 10 min observation period. Administration of each dose of fluphenazine caused complete immobility for 6 to 7 hr. At 48 hr after withdrawal, the rats treated for 28 wks showed a decrease in immobility, and an increase in washing and irritability. Renewed treatment with fluphenazine caused a decrease in walking and an increase in immobility, and by the third day of renewed treatment, the rats resembled the control rats. Rats treated with 5mg/kg fluphenazine did not show withdrawal after 15 wks, but did show withdrawal after 18 wks. In the rats treated for 32 wks, the males showed an increase in locomotor and exploratory behavior during withdrawal as well as during renewed treatment, while females showed no withdrawal effect. 5 references.

002579 Ueno, Takeji. Department of Psychiatry and Neurology, Hokkaido University School of Medicine, Sapporo, Japan **Pathological studies on the brain lesions of rats induced by chronic administration of disulfiram -- with special reference to the ultrastructural aspects of disulfiram psychosis.** Psychiatria et Neurologia Japonica (Tokyo). 78(7):503-520, 1976.

In order to determine if tetraethylthiuram disulfide (Disulfiram) sometimes induces a psychosis during treatment of chronic alcoholism, rats were given the drug and the cerebral cortex, cerebral white matter, and the hypothalamus were examined with light and electron microscopes. With the light microscope, shrinkage of nerve cells was observed in the third layer of the parietal and temporal cortex to various extents. Findings with the electron microscope included: 1) dilated Golgi apparatus; 2) swollen and vacuolated mitochondria with fragmented cristae; 3) more advanced alterations of hypothalamus cells; and 4) various kinds of synaptic changes in the hopothalamus but not in the cerebral cortex. Findings indicated that the cytotoxic action of the disulfiram and the synaptic transmission of the hypothalamus was selectively disturbed by its dopamine-beta-hydroxylase inhibiting action. 69 references. (Author abstract modified)

002580 Wang, R. Y.; Gallager, D. W.; Aghajanian, G. K. Departments of Psychiatry and Pharmacology, Yale University School of Medicine, New Haven, CT 06508 **Stimulation of pontine reticular formation suppresses firing of serotonergic neurones in the dorsal raphe.** Nature (London). No. 5584:365-367, 1976.

Experimentation with rats indicates that stimulation of the pontine reticular formation (PRF) markedly suppresses the activity of the 5-hydroxytryptamine (5-HT) cells in the dorsal raphe nucleus (DRN) and that this effect might be mediated through a PRF-DRN GABAergic pathway. Results support the hypothesis that immediately preceding the onset of and continuing throughout the desynchronized sleep episode, cells in the PRF exert a powerful, inhibitory influence on 5-HT cells in the DRN. On the other hand, it is concluded that the locus coeruleus has a minor and possibly indirect influence on 5-HT cells in the DRN. 25 references.

002581 Willson, N. J.; Schneider, J. F.; Roizin, L.; Fleiss, J. F.; Rivers, W.; Demartini, J. E. Department of Pathology, College of Physicians and Surgeons, Columbia University, New York, NY **Effects of methadone hydrochloride on the growth of organotypic cerebellar cultures prepared from methadone-tolerant and control rats.** Journal of Pharmacology and Experimental Therapeutics. 199(2):368-374, 1976.

The effects of methadone hydrochloride on the growth of organotypic cerebellar cultures prepared from methadone tolerant Sprague-Dawley rats were studied. Results of organotypic cerebellar culture experiments from over 200 rats revealed that the addition of methadone to the medium reduced explant outgrowth size in a dose related effect. There was no significant difference in the effect of methadone on the growth of cultures prepared from methadone tolerant and control animals, but explants prepared from pups of methadone treated mothers showed significantly less outgrowth from explants than did controls. In vivo tests showed that pups from methadone treated mothers tolerated methadone better than those of untreated mothers. This tends to support previous studies indicating that drug tolerance can develop in utero. The observation of growth inhibition of central nervous system tissues by methadone raises questions concerning the advisability of chronic methadone use during pregnancy, even in a therapeutic setting. 25 references. (Author abstract modified)

06 METHODS DEVELOPMENT

002582 Balynina, Ye. S.; Berezovskaya, I. V. Institut gigiyeny truda i profzabolevaniy AMN SSSR, Moscow, USSR **/Comparative evaluation of methods for determining the orientation reaction of rats in a toxicological experiment./** Sravnitel'naya otsenka metodov opredeleniya orientirovochnoy reaktsii krys v toksicologicheskom eksperimente. Farmakologiya i Toksicologiya (Moskva). 39(5):635-638, 1976.

A simple, economical method was sought to establish the orientation reflex as an index of neurotoxic effect of chemical agents, using phthalates and carboran. A modification of previous experiments utilizes an open platform to check the physiological behavior of rats under natural circumstances. The new method is said to be 5 to 10 times more effective than other methods. Thresholds for acute effect were established for dibutyl phthalate, dioctyl phthalate, and carboran. 9 references.

002583 Bickel, M. H.; Weder, H. G. Medizinisch-chemisches Institut, University of Berne, Berne, Switzerland **Characterization of interactions of phenothiazines and related drugs with lipids by UV-spectrophotometry.** Psychopharmacology Communications. 2(3):231-240, 1976.

The characterization of interactions of phenothiazines and related drugs with lipids by UV-spectrophotometry is described. The UV-spectrum of chlorpromazine undergoes a red shift in the presence of vesicles of biological membranes or phospholipids, triglycerides, serum lipoproteins, or fatty acids. The resulting difference spectrum has two positive peaks at about 260 and 320 nm and two negative peaks at 250 and 290nm. This interaction signal, which was elicited in the presence of as little as 3 micromoles oleic acid, was dependent on the concentrations of both ligand and binder. It was abolished by 8 M urea, diminished by temperature increase up to 70 degrees C, but not changed by varying the ionic strength from 0 to 0.5. The chlorpromazine/triglyceride interaction signal was strongly enhanced with pH increasing from 6 to 10. The signal was only obtained with ligands fulfilling specific structural requirements, e.g.,phenothiazines and most iminostilbenes, but not carbamazepine, imipramine, and amitriptyline. 8 references. (Author abstract)

002584 Cheney, D. L.; Costa, E. Laboratory of Preclinical Pharmacology, NIMH, Saint Elizabeths Hospital, Washington, DC 20032 **The transsynaptic regulation of acetylcholine metabolism in nuclei of rat brain: pharmacological implications. (Unpublished paper).** Washington, DC, NIMH, 1976. 30 p.

A series of research methodologies for the measurement of acetylcholine (Ach) and choline (CH) content and turnover rate in rat brain nuclei during cholinergic and monoaminergic interactions are presented. Research findings on cholinergic and dopaminergic interactions in the neostriatum and the nucleus accumbens are reviewed. A series of experiments utilizing radioactive and stable isotope labeling to measure Ach turnover rates and an examination the transsynaptic regulation of Ach metabolism utilizing chlorpromazine, haloperidol and clozapine and narcotic analgesics indicated that the metabolism of Ach may be modulated through dopaminergic postsynaptic receptors in striatum and through enkephalin receptors in hippocampus, nucleus accumbens, and cortex as well as the manner in which direct measurements of Ach turnover rates may be used to investigate neurotransmitter interactions and to describe profiles of drug actions. It is suggested that this analytic approach may prove valuable in the localization of the therapeutic action and side-effects of various drugs. 73 references.

002585 Hill, Shirley Y.; Powell, Barbara J. Dept. of Psychiatry, Washington University School of Medicine, 4940 Audubon Ave., St. Louis, MO 63110 **Cocaine and morphine**

self-administration: effects of differential rearing. Pharmacology Biochemistry and Behavior. 5(6):701-704, 1976.

To investigate the effects of differential rearing on cocaine and morphine self-administration, 2 groups of Wistar rats were reared in either enriched or impoverished conditions for 100 days postweaning. These two groups were further divided and tested for cocaine or morphine preference in a two/bottle choice (water alternative) for 16 days. Enriched and impoverished rearing has previously been found to alter emotionality, conditionability, and body weight of adult rats. Validating previous reports of differential rearing effects on body weight, the enriched animals in the present study weighted less than their litter mates reared in impoverished conditions. Animals reared in the enriched environment consumed significantly more cocaine than animals reared in an impoverished one. No significant differences were observed for morphine self-selection as a result of differential rearing. 19 references. (Author abstract)

002586 Ishitani, Ryoichi; Saito, Ryoko; Miyakawa, Akihisa; Iwamoto, Takio. Department of Pharmacology, Faculty of Pharmaceutical Sciences, Josai University, Saitama 350-02, Japan **Application of energy-dispersion X-ray analysis to electron microscopic autoradiography: distribution of psychotropic drugs in the central nervous system.** Japanese Journal of Pharmacology (Kyoto). 26(Supplement):69P, 1976.

At the 49th general meeting of the Japanese Pharmacological Society, Osaka, Japan, in March, 1976, a study in which electron probe X-ray microanalysis was used to analyze the autoradiographic grains developed during investigation of the cellular distribution of radiolabeled dimetacrine in rat cerebral cortex was reported. Originally, it could not be determined whether or not the grains were silver grain. Analyses with an electron microscope equipped with an energy dispersive microanalyzing system revealed characteristic peaks of lead, silicon and chlorine as elements other than silver. It is suggested that identification of the resultant grains must be performed when high resolution autoradiography is done. (Author abstract modified)

002587 Walters, Judith R.; Roth, Robert H. Natioanl Institute of Neurological and Communicative Disorders and Stroke, NIH, Bethesda, MD 20014 **Dopaminergic neurons: an in vivo system for measuring drug interactions with presynaptic receptors.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 296(1):5-14, 1976.

An in vivo system was used to investigate the ability of dopamine agonists and antagonists to alter dopamine synthesis by acting at what appear to be presynaptic dopamine receptors. To eliminate psotsynaptically induced changes in dopamine synthesis caused by the effects of these drugs on the firing rate of dopamine neurons, gamma-butyrolactone was administered to block impulse flow in the nigro/neostriatal pathway. The accumulation of Dopa in the rat striatum after administration of Dopa decarboxylase inhibitor was used as an index of striatal tyrosine hydroxylase activity. It was found that administration of the dopamine agonists, apomorphine or ET-495 (1-(2'-pyrimidyl)-piperonyl-piperazine), modified the apparent activity of striatal tyrosine hydroxylase when impulse flow was blocked in dopamine neurons. This presynaptic effect of apomorphine could be prevented by low doses of loxapine haloperidol and spiroperidol. Chlorpromazine, fluphenazine, and thioridizine were much less effective than the butyrophenones in blocking the effects of apomorphine. Molindone and (+)butaclamol, but not (-)butaclamol, reversed the presynaptic agonist effects, pimozide was a weak blocker and clozapine had no effect. All these neuroleptics except (-) butaclamol caused a significant increase in Dopa accumulation when impulse flow was intact. Compared with haloperidol the phenothiazines and pimozide appeared less potent in reversing the presynaptic effects of apomorphine than in blocking the behavioral effects of this agonist. Possible functional significance of the presynaptic dopamine receptors are considered. 52 references. (Author abstract)

07 EARLY CLINICAL DRUG TRIALS

002588 Ambrozi, L.; Birkmayer, W.; Riederer, P.; Youdim, M. B. H. Ludwig Boltzmann Neurochemistry Institute, A-1130 Vienna-Lainz, Austria **L-Dopa and (-)-deprenil in the treatment of Parkinson's disease: a long-term study.** British Journal of Pharmacology (London). 58(3):423P-424P, 1976.

In a paper presented at a meeting of the British and French Pharmacological Societies, Sept. 1976, at Oxford, England, the long-term effects of Madopar (L-dopa and the peripheral decarboxylase inhibitor Benseracide (N-1, DL-seryl-N-2, (2,3,4-trihydroxybenzyl) hydrazine plus (-)-deprenil were studied. Subjects were 223 Parkinsonian patients. Intravenous (i.v.)therapy was more effective than oral therapy, but side-effects occurred more often with i.v. and to a greater extent, and i.v. was discontinued. The addition of deprenil to Madopar therapy resulted in a significant reduction in patients' functional disability. Abnormal involuntary movements occurred in 16, psychosis in 14, orthostatic hypotension in 5 and nausea in 8. Reduction of the deprenil dose resulted in the disappearance of some of the side-effects. effects. The therapy produced no response in 13.9% of patients. The improvement of disability following deprenil occurred within 20 to 120 min after a single dose and lasted for 1 to 3 days. Thus it may act not only by inhibiting monoamine oxidase, but also as a psychostimulant by releasing dopamine in a fashion similar to amphetamine. The improvement of disability was independent of the duration of the illness and the results indicate that the inclusion of deprenil leads to a better utilization of synthesized dopamine from L-dopa. 6 references.

002589 Bonierbale, M.; Dufour, H.; Scotto, J. C.; Sutter, J. M. Hopital de la Timone, F-13385 Marseilles, France **/Metapramine as antidepressant and psychostimulant./** La metapramine, antidepresseur et psycho-stimulant. Encephale (Paris). 2(3):219-223, 1976.

The results of a clinical trial of metapramine, a tricyclic antidepressant, were presented at the 10es Journees d'Information Psychiatrique, Marseilles, 1976. Good or excellent results were obtained in 16 of 24 patients with melancholia, 5 of 9 patients with involutional melancholia, 23 of 40 patients with neurotic depression or reactive depression, and 5 of 8 patients with psychotic depression. At the end of 3 weeks, there was a significant decrease in depressed mood, suicidal thoughts, hypochondria, and guilt feelings. There was also a significant decrease in patients' ratings on the Hamilton Scale both after 1 week and 3 weeks. Metapramine also had a psychostimulant effect, significantly reducing mental inhibition, motor inhibition, and somatic anxiety, and nonsignificantly reducing mental anxiety. The drug was well tolerated by the patients.

002590 Broughton, Roger; Mamelak, Mortimer. Faculte de Medicine, Departement de Medecine (Neurologie), Hopital General, Universite d'Ottawa, Ottawa, Canada **Gamma-hydroxy-butyrate in the treatment of narcolepsy: a preliminary report.** In: Guilleminault, C., Narcolepsy: proceedings. New York, Spectrum, 1976. 707 p. (p. 659-667).

In a paper given at the First International Symposium on Narcolepsy, Montpellier, France, July 1975, the use of gamma-hydroxy-butyrate in treatment of narcolepsy was evaluated in four patients with long-term histories of idiopathic narcolepsy with cataplexy. All night sleep recordings were made on two patients, and ambulatory recordings were made on two patients during two to three placebo or baseline nights followed by a week or more of treatment with gamma-hydroxy-butyrate, and then 2 or more placebo nights. Clinical changes were apparent after three or four nights of treatment, diurnal irresistible sleep attacks and cataplexy disappeared, and patients coped better with chores and had improved moods. Daytime vigilance remained impaired, and patients continued diurnal sleepiness. Nocturnal dyssomnia returned as soon as the drug was discontinued, and diurnal sleep attacks and cataplexy reappeared within one to three days. The drug increased total nocturnal sleep time, decreased nocturnal wakefulness, increased delta sleep, increased duration and proportion of nocturnal rapid eye movement sleep, and decreased rapid eye movement density. It was tentatively concluded that gamma-hydroxy-butyrate favorably modified the course of compound narcolepsy because daytime symptoms were secondary to nocturnal sleep disturbance. 29 references.

002591 Brown, H. Colin; Carruthers, S. George; Johnston, G. Dennis; Kelly, John G.; McAinsh, James; McDevitt, Denis G.; Shanks, Robin G. Dept. of Therapeutics, Queen's University of Belfast, 97 Lisburn Rd., Belfast BT9 7BL, Northern Ireland **Clinical pharmacologic observations on atenolol, a beta-adrenoceptor blocker.** Clinical Pharmacology and Therapeutics. 20(5):524-534, 1976.

The effects of oral and intravenous administraton of atenolol were studied in healthy volunteers. The oral administration of a series of single doses of atenolol reduced an exercise tachycardia. After a 200mg dose, the effect on an exercise tachycardia was maximal at 3 hours and declined linearly with time at a rate of approximately 10% per 24 hours. The peak plasma atenolol concentration occurred at 3 hours and therafter declined exponentially with time with an elimination half-life of the dose excreted in urine within 72 hours. There was a correlation between the reduction in an exercise tachycardia and the logarithm of the corresponding plasma concentration. The intravenous administration of atenolol reduced exercise tachycardia with a significant correlation between effect and plasma concentration. After 50mg intravenously, 100% of the dose was recovered from the urine, and the clearance was 97.3ml/minute. Comparison of area under the curve after oral and intravenous administration showed the bioavailability to be 63% after oral drug. Repeated oral administation of atenolol 200mg daily either as a single dose or in divided 12 hourly doses for 8 days maintained reduction of an exercise tachycardia of at least 24% during the period of drug administration. The plasma elimination half-life, area under the plasma concentration time curve, and peak plasma concentration after 200mg atenolol were not changed by chronic dosing for 8 days. 10 references. (Author abstract modified)

002592 Calne, D. B.; Kartzinel, R.; Shoulson, Ira. National Institute of Neurological and Communicative Disorders and Stroke, National Institutes of Health, Bethesda, MD 20014 **An ergot derivative in the treatment of Parkinson's disease.** Postgraduate Medical Journal (Oxford). 52(Supplement 1):81-82, 1976.

In a paper presented at a symposium on ergot compounds in London in May 1975, studies were reported establishing the

therapeutic action of bromocriptine in Parkinsonism. It is noted that the drug is likely to prove a valuable addition to current forms of treatment, provided long-term administration is tolerated without generating any major toxicological problem. The advent of a transmitter agonist as routine therapy represents a novel approach to the management of neurological disease which may, with further experience, shed new light on disturbances underlying the pathophysiology of central synaptic mechanisms in man. 11 references. (Author abstract modified)

002593 Carrere, J.; Roux, J.-M. Hopital Psychiatrique de Villejuif, 54, avenue de la Republique, F-94800 Villejuif, France **/Sulpiride in withdrawal of nonalcoholic drug addicts./** Le Sulpiride dans le sevrage des toxicomanies non ethyliques. Annales Medico-Psychologiques (Paris). 1(2):266-271, 1976.

The use of sulpiride (Dogmatil) in treatment of withdrawal symptoms in drug addicts was discussed at a meeting of the Societe Medico-Psychologique held on January 26, 1976. A group of 17 patients, including 16 males, who had been taking drugs i.v. for 5 to 12 years, were hospitalized and given 600mg t.i.d. of sulpiride i.v. After the first few days, the dose of sulpiride was decreased to 1200mg/day po, then 600mg/day, and after the first week the dose was further reduced to 200 to 600mg/day, which was maintained for several days. Other drugs given were pethidine in low doses, chlorazepate up to 150mg/day, antiparkinson agents, hypnotics, and vitamins. Of the 17 patients, 14 were addicted to opiates, 1 to amphetamine and cocaine, and 2 to LSD. In the opiate addicts, attenuation of the withdrawal state was total in 4, good in 10, and slight in 1. Side-effects of sulpiride were extrapyramidal symptoms, difficulty in accommodation, orthostatic hypotension, and euphoria. 9 references.

002594 Cole, Jonathan O. Department of Psychiatry, Temple University, Philadelphia, PA **The clinical evaluation of new drugs.** In: Advances in the drug therapy of mental illness. Geneva, World Health Organization, 1976. 168 p. (p. 43-44).

A brief overview of the development and clinical evaluation of new drugs for the treatment of psychiatric conditions is presented. The lack of discoveries of potent new drugs in the US during 1971-1976 is discussed and possible causes for this situation are outlined. It is felt that a better knowledge of blood levels of known drugs or of their biochemical or electrophysiological mechanisms of action will lead to substantial gains in efficiency, and that existing methods for measuring the effects of new psychoactive drugs are adequate for identifying new potent agents that may be useful in treating anxiety, depression, schizophrenia or even chronic organic psychoses. The public attitude against human experimentation is presented as the major inhibitor of new drug discovery and testing.

002595 Feldmann, Harry; Denber, Hermann C. B. 15, Avenue Krieg, Geneva, Switzerland **/AHR 6134: a new antianxiety drug with unexpected results./** AHR 6134: Nouvel anxiolytique a resultats inattendus. Annales Medico-Psychologiques (Paris). 2(2):269-279, 1976.

A clinical trail of AHR 6134, a derivative of lenperone with a spectrum of activity resembling the butyrophenones, was reported at the June 1976 meeting of the Societe Medico-Psychologique. The drug was given to 22 females and 6 males, 16 to 69 years old, with a target symptom of anxiety. Diagnoses were neurosis in 19, reaction following cranial trauma in 2, depression with anxiety in 5, and schizophrenia in 2. The dose of AHR 6134 varied from 1.5mg/day to 10mg/day. Patients were evaluated by the Hamilton Anxiety Rating Scale and the Brief Psychiatric Rating Scale. Laboratory tests included blood count, sedimentation rate, BUN, SGOT, alkaline phosphatase, urinalysis, and EKG. Treatment ranged from 1 to 74 days, with a mode of 21 to 30 days. Generally, the drug showed rapid anxiolytic action. However, in 7 patients, there was an aggravation of symptoms. Results were excellent in 10, very good in 4, good in 8, unchanged in 1, and worse in 5. Headache occurred in 6 patients, visual problems in 3, and dry mouth and nasal stuffiness in 2. Case reports are given for 7 patients.

002596 Fracassi, Marcelo J.; Delvecchio, Fernando R. Corrientes 933, Rosario, Argentina **/Clinical evaluation of a weekly administered neuroleptic: Penfluridol (R16341)./** Evaluacion clinica de un neuroleptico semanal de mantenimiento: Penfluridol (R16341). Acta Psiquiatrica y Psicologica de America Latina (Buenos Aires). 22(4):302-305, 1976.

To establish some therapeutic guidelines for the use of penfluridol (R16341), 26 patients, 15 women and 11 men, ages 17 to 63 years, were treated with this neuroleptic drug in an open study. All the subjects were psychotic, and 22 were diagnosed as schizophrenic (17 paranoid, 3 simple, and 2 hebephrenic). The experiment was begun by administering one weekly dose of 20mg. The maximum study period for each patient was 100 days, during which the dosage was adjusted according to patient response. Clinical and statistical evaluations were used. Therapeutic dosages were established at between 10 and 80mg, with 20mg per week as the usual dose in 42% of the cases. The results showed improvement in hallucinations and delirious ideation and concomitant positive effects on the symptoms of mistrust and affective withdrawal. This was reflected in improved relationships and handling of crisis situations. The prolonged therapeutic action also made it easier for patients to reduce drug intake. 16 references.

002597 Genevieve, J.-M.; Couriol, A. Hopital Psychiatrique Sainte-Marie de l'Assomption, F-07000 Privas, France **/First clinical impressions after use of sultopride for treatment of manic states of agitation./** Premieres impressions cliniques apres l'utilisation du sultopride pour le traitement d'etats d'agitation maniaque. Semaine des Hopitaux Therapeutique (Paris). 52(5-6):329-330, 1976.

Sultopride (Barnetil) was studied in 5 manic agitated patients, 4 males and 1 female, 19 to 48 years old. The dose varied from 1600mg to 4000mg, and duration of treatment ranged from 10 to 200 days. Very good results were obtained in 2 cases, good results in 1 case, and no change in 2 cases. One of those failing to respond to sultopride responded well to haloperidol. There was no difference in response between typical manics and atypical manics. The two patients responding very well developed extrapyramidal symptoms, which responded well to antiparkinson medication.

002598 Goldstein, S. E.; Birnbom, F. Department of Psychiatry, Queensway-Carleton Hospital, 60 Larkspur Drive, Ottawa, Ontario K2H 6L1, Canada **Piperacetazine versus thioridazine in the treatment of organic brain disease: a controlled double-blind study.** Journal of the American Geriatrics Society. 24(8):355-358, 1976.

In a double-blind crossover study, 50 geriatric patients with organic brain disease were divided into two groups. One group first received piperacetazine for 15 days and then thioridazine for 15 days. For the other group the sequence was reversed. Piperacetazine proved to be at least as effective as thioridazine and seemed to be more effective against certain

target symptoms; side-effects were less common and less severe. 9 references. (Journal abstract)

002599 Greenblatt, David J.; Shader, R. I.; Koch-Weser, J. Clinical Pharmacology Unit, Massachusetts General Hospital, Boston, MA 02114 **The psychopharmacology of beta adrenergic blockade: pharmacokinetic and epidemiologic aspects.** In: Carlsson, C., Neuro-psychiatric effects of adrenergic beta-receptor. Munich, Urban & Schwarzenburg, 1976. 120 p. (p. 6-13).

In a paper presented at a symposium on neuropsychiatric effects of adrenergic beta-receptor blocking agents held in Copenhagen, October, 1975, propranolol and practolol are examined with respect to their neurological effects through their pharmacokinetic properties and their potential applications in treating anxiety, tremor, drug addiction and withdrawal, acute adverse reactions to drugs of abuse, antidepressant poisoning, essential circulatory hyperkinesis, and stuttering. It is concluded that both drugs could have direct effects upon the central nervous system. This conclusion is supported by epidemiologic surveys of unwanted neuropsychiatric effects attributed to these drugs in both hospitalized and ambulatory patients. 42 references.

002600 Kartzinel, Ronald; Calne, Donald B. Laboratory of Neuropharmacology, National Institute of Neurological and Communicative Disorders and Stroke, NIH, Bethesda, MD 20014 **Studies with bromocriptine: Part 1. "On-off" phenomena.** Neurology. 26(6,Pt.1):508-510, 1976.

A dopaminergic agonist, bromocriptine, has been studied in patients with idiopathic parkinsonism complicated by severe "on-off" phenomena induced by levodopa. In a "blind" self-evaluating within patient comparison, fluctuations in clinical state still occurred when levodopa (with or without carbidopa) was replaced with bromocriptine, but they were significantly reduced in frequency. The observation that on-off phenomena can be induced by bromocriptine complicates interpretation of these episodes in terms of pharmacokinetics of levodopa. There may be variations in receptor sensitivity or alterations in the influence of unidentified neurophysiologic mechanisms that modulate striatal output. 22 references. (Journal abstract)

002601 Lewicka-Wysocka, Hanna; Zajaczkowska, Anna; Kojecka, Izabella; Wolak, Ewa; Piotrowski, Zygmunt; Wardaszko-Lyskowska, Halina. Klinuka Psychiatryczna, Akademia Medyczna, Warsaw, Poland **/Results of Leponex treatment./** Wyniki Leczenia Leponexem. Psychofarmakoterapia Schizofrenii Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 253-256).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, results of antipsychotic treatment using Leponex (Sandoz proprietary name for clozapine) are presented. The clinical investigations, conducted with the cooperation of Sandoz, were carried out on a group of 13 patients with various forms of psychomotor disorders. The study shows that the drug is very fast acting, and produces strong tranquilizing effects. Among the side-effects noted were raised body temperature and feelings of fatigue and dizziness. Parkinsonian symptoms were not observed. The study concludes that Leponex is a drug with considerable promise which should be more fully tested in the future. 5 references.

002602 Linke, H. Kurklinik Pitzer, Genthstr. 7/9, D-6208 Bad Schwalbach/Taunus, Germany **/Obesity as a therapeutic problem: experience with the appetite depressant Mazindol./** Die Ubergewichtigkeit als therapeutisches Problem: Erfahrungen mit dem Appetithemmer Mazindol. Medizinische Welt (Stuttgart). 27(42):2021-2025, 1976.

The efficacy of the appetite depressant Mazindol (5-p-chlorophenyl-2,3-dihydro-3H-imidazo(2,1-a)isoindol-5-ol) in the treatment of obesity was investigated. Eighty patients with predominantly alimentary type adiposity with at least 20% excess weight were treated for 4 weeks. Maxindol was administered once daily in a dosage of 2mg, 1 hour before lunch. Of the 80 patients, 60 were placed on a reducing diet of 800-1200 calories; the other patients received about 2500 calories in normal meals. A comprehensive series of laboratory tests was conducted at weekly intervals. Average weight loss of dieting patients after 4 weeks was 6kg; patients on normal food intake lost an average of 5.9kg. Most patients continued on reduced caloric intake even after withdrawal of the anorexic. Eight patients terminated therapy because of side effects; these included dryness of the mouth, insomnia, vertigo, nervousness, headache, fatigue, tendency to perspiration, and similar manifestations. It is concluded that Mazindol is a reliable appetite depressant for temporary application when dietary and psychotherapeutic measures do not suffice.

002603 Planche, R. C.H.U. de Clermont-Ferrand, Clermont-Ferrand, France **/The place of sultopride among neuroleptic cures./** Place du sultopride dans les cures neuroleptiques. Annales Medico-Psychologiques (Paris). 2(3):512, 1976.

A report on the use of sultopride in 40 patients was presented to the 1976 session of the Societe de Psychiatrie, Neurologie et Psychologie Clinique du Centre, Auvergne et Limousin. The favored indication of this drug is acute psychotic crisis. Sultopride rapidly reduces maladapted and delirious excitation, facilitating a psychotherapeutic approach. Its rapidity of action is equal to that of the better neuroleptics used in the treatment of acute states. The combination of a sedative and antipsychotic action is comparable to that achieved by a combination of haloperidol and injectable Nozinan. In 40% of the patients studied, a depressive effect appeared after about a month. Thus, for more prolonged treatment, sultopride should be progressively replaced by moderate or strong doses of sulpiride or by a long-acting neuroleptic.

002604 Ritschel, W. A. College of Pharmacy, University of Cincinnati Medical Center, Cincinnati, OH 45221 **Pharmacokinetic approach to drug dosing in the aged.** Journal of the American Geriatrics Society. 24(8):344-354, 1976.

A theory mandating the pharmacokinetic approach to dosimetry for the aged is presented. Data in the literature show that there is a constant ratio of total body fluid to lean cell mass with increasing age (1.15 for males and 1.31 for females). Since drug receptors usually are found in the tissues, and since cell mass and total body fluid apparently decrease at a constant rate, it would seem that the volume of distribution of drugs decreases proportionally with increasing age. Kidney function, as measured by the glomerular filtration rate and transport maximum, apparently decreases with increasing age according to zero order kinetics. Based on these data, correction factors were established for the change in volume of distribution and renal functions with increasing age. Equations were derived for calculating the loading dose and maintenance dosage of drugs in multiple dose therapy in females and males. Equations are presented for drugs following the minimal inhibitory concentration (MIC) pattern and the log dose response pattern, respectively. The MIC pattern is recommended in the use of bacteriostatic drugs, for which it is essential to maintain during the entire course of therapy a minimum inhibitory con-

centration. The log dose response pattern is recommended for bactericidal and antiarrhythmia drugs, for which it is essential to obtain an average therapeutic steady state concentration. Based on this pharmacokinetic approach, it would seem that elderly patients, during multiple dose therapy, are exposed to dose sizes that are too large if no correction is made. 49 references. (Journal abstract modified)

002605 Seitz, Heinz. Psychiatrisches Krankenhaus, D-6253 Hadamar, Germany **/Experiences with Juston in patients with depressive and dystonic affect./** Erfahrungen mit Juston bei Patienten mit depressiven und dystonen Affekten. Therapie der Gegenwart (Munchen). 115(9):1566-1567, 1570-1572, 1976.

Juston, a medication containing 300mg/capsule 1-hexyl-3,7-dimethylxanthine with a multivitamin was studied in 30 patients averaging 54 years of age, who suffered from cerebral sclerosis, reactive depression, exogenous psychoses following alcohol or drug abuse, and schizophrenia with depressive mood. A total of 11 patients had been ill less than 6 months, while 11 had been ill from 6 months to 3 years, and 6 had been ill more than 3 years. Patients received 1 to 4 capsules of Juston daily for 8 weeks. Rating with the Wechsler Depression Questionnaire showed full recovery in 22 patients, partial success in 3 patients, and no improvement in 5 patients. In no case did treatment have to be interrupted because of side-effects. 7 references.

002606 Wyper, D. J.; McAlpine, C. J.; Jawad, K.; Jennett, B. MRC Cerebral Circulation Research Group, Institute of Neurological Sciences, Southern General Hospital, Glasgow, Scotland **Effects of a carbonic anhydrase inhibitor on cerebral blood flow in geriatric patients.** Journal of Neurology, Neurosurgery, and Psychiatry (London). 39(9):885-889, 1976.

Carbonic anhydrase inhibitors (CAI) were investigated for their vasodilatory effect. CAI was shown to increase cerebral blood flow in mildly demented geriatric patients. It was determined that CAI (UK-12,130) has a more selective action on the brain, and because it crosses the blood-brain barrier more readily it is more lipophilic and has lower ionization compared with acetazolamide. Oral administration caused a significant increase in blood flow at two different dose levels; this increase persisted for at least 6 weeks, the duration of the longest study. There was no consistent improvement in mentation during treatment. Blood flow was measured by the washout of 133Xe after inhalation of this inert gas. 11 references. (Author abstract modified)

002607 Yorkston, Neil J.; Zaki, Saniha A.; Themen, Judith F. A.; Havard, C. W. H. no address **Safeguards in the treatment of schizophrenia with propranolol.** Postgraduate Medical Journal (Oxford). 52(Supplement 4):175-180, 1976.

Some practical safeguards in the treatment of schizophrenics with propranolol are outlined. Early results from an uncontrolled study of 55 patients with florid schizophrenia suggest that propranolol can be used safely in high dosage, and in a proportion of cases it appears to control schizophrenic symptoms. Evidence from this uncontrolled study suggests that there was a therapeutic dose range in which symptoms steadily improved, as a low dose was ineffective and a high dose, particularly if reached too rapidly, caused toxic effects. Rapid increases (400 to 800 mg) in the daily total intake when given in divided doses (4 to 10/day) produced gross toxic effects that included ataxia with unprotected falls, drop attacks, visual hallucinations, and confusional states. Severe toxic effects were uncommon when the dose was raised by regular, gradual increments (e.g. by 40 to 80 mg/day), when propranolol was given twice daily, when the dose was held steady as the patient started to improve, and when the daily total dose was reduced if the fall in pulse rate or blood pressure was excessive, or if there was evidence of toxicity. The observation of gradual, progressive improvement was the most valuable positive guide to the dose of propranolol. All schizophrenic symptoms remitted, at least temporarily, in 26 of 55 patients. Patients who then stopped propanolol usually relapsed within hours or days. It was concluded that controlled studies of propranolol in schizophrenic patients are indicated. 7 references. (Author abstract modified)

08 DRUG TRIALS IN SCHIZOPHRENIA

002608 Afeltowicz, Zbigniew; Sep-Kowalikowa, Barbara; Zgirski, Ludomir. Klinika Psychiatryczna AM, ul. Debinki 7, 80-211 Gdansk, Poland **/Comparative study of the therapeutic effectiveness of Mirenil Prolongatum and Moditen Depot in treatment of schizophrenia./** Porownawcza ocena efektywnosci mirenilu prolongatum i modeteny depot w leczeniu psychoz schizofrenicznych. Psychiatria Polska (Warszawa). 10(5):479-485, 1976.

A comparative study was made of the therapeutic effectiveness of Mirenil Prolongatum and Moditen Depot in treatment of schizophrenia, based on results with a group of 36 patients (14 males, 22 females), who were treated with Moditen Depot, and a group of 32 patients (15 males, 17 females), who were treated with Mirenil Prolongatum. In the Moditen group seven patients did not respond to treatment, while in the Mirenil group four patients did not improve and three deteriorated. Symptoms of Parkinsonism were observed in both groups, with 30 cases in the former and 25 cases in the latter. Therapeutic efficacy of both drugs was similar. Both acted best in cases of ample psychnotic production and in chronic schzophrenic syndromes, where they improved affective contact of the patients and stimulated their psychomotor activity. 14 references. (Journal abstract modified)

002609 Ando, Susumu. Musashi National Sanatorium, Tokyo, Japan **Follow-up of patients with chronic schizophrenia -- with special reference to the effects of pharmacotherapy.** Iryo (Tokyo). 30(7):639-646, 1976.

The results of a survey of 529 chronic schizophrenia patients in Japanese national hospitals and as outpatients, 10 or more years after onset of schizophrenia are presented to clarify the effects of pharmacotherapy. Five hundred and four of the patients had shown little or no progress since the onset of their chronic schizophrenia. The effectiveness of shock therapy diminished with the length of the disease. When pharmacotherapy was begun early, the cases requiring confinement could be reduced. The frequency of improvement among confined patients due to pharmacotherapy was higher among those who had required constant supervision, than those who could perform simple unsupervised tasks. It was felt that the study was significant in that for more than 500 patients the effectiveness of pharmacotherapy could be assessed. 30 references. (Journal abstract modified)

002610 Aria, M.; Marzo, M.; Spadaro, P. Ospedale Psichiatrico Provinciale di Catanzaro in Girifalco, Catanzaro in Girifalco, Italy **/Fluphenazine decanoate in chronic psychotic subjects./** Il decanoato di flufenazina in soggetti psicotici lungodegenti. Rivista Sperimentale di Freniatria (Reggio Emilia). 100(5):1211-1225, 1976.

A trial of fluphenazine decanoate in long-term institutionalized psychotic patients is reported. The group of 57 male and

15 female patients had an average age of 44. Most were schizophrenic, and all had been receiving other psychopharmacologic agents, electroconvulsive therapy and insulin shock. Results showed modification of autistic traits, and psychotic personality disorders, and resocialization was achieved in some cases. It is concluded that fluphenazine is a long-acting neuroleptic that is especially useful in treating outpatients. 24 references.

002611 Ayd, Frank J. no address **Therapy with injectable fluphenazines.** Current Psychiatric Therapies. 16:177-189, 1976.

Data from administration of depot fluphenazines to patients worldwide, over the past 10 years, in doses at intervals ranging from a few hours to 8 weeks, and for periods of up to 7 years, are summarized. Clinical indications for the depot fluphenazines are seen as including inpatient or outpatient chronic schizophrenics, newly admitted acute schizophrenic patients, and patients with other acute psychoses in some cases. Effect pharmacotherapy with depot fluphenazines is described; it includes the injection of the lowest effective dose as infrequently as possible. Side-effects have included minor autonomic effects, infrequent hypotensive episodes, sporadic dermatologic disorders, and varying degrees of drowsiness and lethargy. Neurophysiologic effects such as akinesia, dyskinesia, akathisia, and Parkinsonism are discussed. It was found that there is little reason to fear adverse reactions with other drugs. It is concluded that increasing numbers of psychiatric patients will be treated with long acting oral and injectable fluphenezines preparations, for scientific reasons, and because of mounting pressure to provide outpatient mental health care expeditiously, safely, and economically. 33 references.

002612 Bach, Otto; Petermann, Harald; Heber, Ilka. Psychiatrische Klinik der Karl-Marx Universitat, Emilienstr. 14, DDR-701 Leipzig, Germany **/Experience with the use of Sydnocarb, a new psychostimulant./** Erfahrungen mit einem neuen psychostimulierenden Medikament-Sydnocarb. Psychiatrie Neurologie und Medizinische Psychologie (Leipzig). 28(10):609-614, 1976.

Administration of Sydnocarb, a new psychostimulant for use in treating schizophrenia, is described. The Soviet drug, N-phenylcarbamoylphenylisopropylsydonomine, was tested in 28 psychotic patients, including 13 with schizophrenia, 4 with brain damage, and 11 neurotics with neurasthenic symptomology. The drug was found to produce good to very good results in 21 of the 25 patients with psychomotor agitation and in 4 of the neurosthenic cases it gave excellent subjective results. Drug therapy had to be interrupted in only two cases. The drug appears to be a better psychostimulant than other available psychopharmacological preparations. 6 references.

002613 Ban, Thomas A. no address **Pharmacotherapy of schizophrenia.** Current Psychiatric Therapies. 16:163-175, 1976.

The treatment of choice for schizophrenia, pharmacotherapy with neuroleptics, is described. It was found that among the actions of neuroleptics, dopamine receptor blockade in the corpus striatum and limbic lobe structures, as well as the resulting increase in dopamine synthesis and turnover rate, was directly related to therapeutic effects. It is noted that while maintenance therapy may prevent relapse, chronic administration of neuroleptics may lead to skin and eye complications or persistent dyskinesia. Clinical effects of neuroleptics are discussed, and developments of drugs with increased neuroleptic potency, diminished mood-depressant property, prolonged duration of action, and decreased frequency of extrapyramidal side-effects are described. A list of additional information sources is provided. 30 references.

002614 Ban, Thomas A. Division of Psychopharmacology, McGill University, Montreal, Canada **Pharmacotherapy of schizophrenia: a critical evaluation.** In: Advances in the drug therapy of mental illness. Geneva, World Health Organization, 1976. 168 p. (p. 23-32).

A review of the literature on the pharmacotherapy of schizophrenia is presented. It is concluded that despite the positive effect of the introduction of chlorpromazine, schizophrenia has remained one of the greatest public health problems in all the civilized countries of the world. Neuroleptics have considerably transformed the prevailing manifestations of the disease, yielding the false contention that schizophrenia does not exist, while changes in social attitude have produced an absolute and relative increase in schizophrenic patients in the community. 84 references.

002615 Bertuzzi, G. L.; Galletti, G.; Peghini, R. Ospedale Psichiatrico della Provincia di Trento, Trento, Italy **/Pipotiazine palmitate in chronic schizophrenia./** Il palmitato di pipotiazina nella schizofrenia cronica. Rivista Sperimentale di Freniatria (Reggio Emilia). 100(5):1226-1238, 1976.

A clinical study was made of pipotiazine palmitate in 19 institutionalized schizophrenics, 24 to 64 years old, demonstrating the long-acting effect of the drug and its acceptable tolerance. Patients were administered the drug for from 40 to 300 days with 180 days being the normal length of treatment. Results show that pipotiazine palmitate permits minimum dependence upon the drug, allows for minimum conflict with other types of therapy, and exhibits better and faster psychotherapeutic and sociotherapeutic resocialization of the patient. The drug can be used for both hospitalized patients and outpatients, is well tolerated and has few if any extrapyramidal effects. 36 references.

002616 Bichonski, Ryszard. Miejskiej Szpital Specjalistycznej, Oddzial Psychiatrii Dzieciecej, Krakow, Poland **/Changes in the physical and chemical properties of blood during pharmacological treatment of schizophrenic children./** Zmiany wlasciwosci fizykochemicznych krwi w procesie leczenia farmakologicznego dzieci schizofrenicznych. Psychofarmakoterapia Schizofrenii Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 189-195).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, a study of physical and chemical properties of blood during pharmacological treatment of schizophrenic children with chloropromazine and haloperidol is presented. Using two groups of children, one healthy, the other schizophrenic, blood changes were examined in response to medication. The characteristic studies were: blood pH, viscosity, surface tension, electrical interphase tension, surface potential and electrical conductance. The study shows that schizophrenic children have lower blood surface tension during chlorpromazene treatment. The interphase tension, and the surface electrical potential are also lower. Haloperidol does not seem to have any effect. The changes however do not appear to be significant and probably do not affect the children's psychological well-being. 11 references.

002617 Bichonski, Ryszard. Miejski Szpital Specjalistyczny, Oddzial Psychiatrii Dzieciecej, Krakow, Poland. **/Change in the interphase electric potential of blood during pharmacological treatment of children for schizophrenia./** Zmiana elektrycznego potencjalu miedzyfazowego krwi w czasie leczenia farmakologicznego dzieci schizofrenicznych. Psychofarmakoterapia Schizofrenii Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 183-188).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, changes in interphase electric potential of blood during pharmacological treatment of children for schizophrenia were described. The study used two groups of children, one healthy, the other schizophrenic. Interphase potential of blood sodium and potassium was measured before and after medication. The study indicates that in schizophrenic children sodium blood plasma increased, whereas the potassium blood plasma factor decreased. Administration of chlorpromazine has the effect of changing these levels, bringing them closer to the healthy children's level. Haloperidol, however does not produce significant changes. 11 references.

002618 Bidzinski, Andrzej; Puzynski, Stanislaw; Bidzinska, Elzbieta; Bojdecki, Krzysztof; Rode, Anna. Instytut Psychoneurologiczny, 1/9 Sobieskiego Al., Warsaw, Poland **/Activity of peripheral blood cholinesterase during pharmacotherapy of schizophrenia./** Aktywnosc obwodowych cholinesteraz w schizofrenii i w czasie jej farmakoterapii. Psychiatria Polska (Warszawa). 10(5):487-496, 1976.

Peripheral blood cholinesterase activity during pharmacotherapy of schizophrenia was studied based on determination of erythrocyte acetylcholinesterase and plasma pseudocholinesterase activity in 36 patients of both sexes diagnosed as paranoid schizophrenics. Results indicate that during treatment with neuroleptics a statistically significant drop in acetylcholinesterase activity took place immediately preceding administration of antiparkinsonian agents. Statistically significant drops in pseudocholinesterase activity were observed only in patients treated with chlorpromazine. No correlation was found between changes in activity of both enzymes with respect to the pretreatment value and clinical improvement after treatment, and a negative correlation between patient age and acetylcholinesterase was demonstrated in this group. 22 references. (Journal abstract modified)

002619 Bilikiewicz, Adam. Klinika Chorob Psychicznych, Akademia Medyczna, Gdansk, Poland **/Personal experience in treating schizophrenic psychosis using fluanxol-depot./** Wlasne doswiadczenia w leczeniu psychoz schizofrenicznych fluanksolem-depot. Psychofarmakoterapia Schizofrenii Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 95-102).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, an experience in treating schizophrenic psychosis using fluanxol depot is described. The study of 20 patients indicates that fluanxol depot is a useful neuroleptic, particularly for patients with low psychomotor drive. The patients exhibited rapid improvement in their emotional condition and the drug was well tolerated. The period of drug action was confirmed as being in the range of 2 to 4 weeks, thus making it an ideal posthospitalization maintenance drug. 12 references.

002620 Bukowczyk, Adam; Wasik, August; Horodnicki, Jan; Janicki, Andrzej. Klinika Psychiatryczna, Akademia Medyczna, Wroclaw, Poland **/Clinical evaluation of Mirenil-Polfa in treating schizophrenic psychosis./** Ocena kliniczna Mirenilu-Polfa w leczeniu psychoz schizofrenicznych. Psychofarmakoterapia Schizofrenii Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 165-171).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drug in Schizophrenics held in Wroclaw, Poland, in October 1973, a clinical evaluation of Miremil, Polfa's proprietary name for fluphenazine, in the treatment of schizophrenic psychosis is presented. In addition to supporting references, data on 34 patients with chronic schizophrenia and 10 patients with hallucinatory schizophrenia indicate that Mirenil is a useful therapeutic agent with tolerable side-effects.

002621 Bukowczyk, Adam; Wasik, August; Brys, Jozef; Domagalski, Jerzy; Kiejna, Andrzej; Horodnicki, Jan. Psychiatric Clinic of the Medical Academy, Wroclaw, Poland **Clinical investigation of clozapine in schizophrenia.** Psychofarmakoterapia Schizofrenii Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 233-252).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, a double-blind study is reported comparing the action of clozapine and chlorpromazine in schizophrenics. Optimum dosage, tolerance and side-effects also were studied. The study showed that clozapine leads to considerable improvement, especially in paranoid hallucinatory schizophrenia, at a lower dosage than other neuroleptics and that its strong antipsychotic effect is not linked with extrapyramidal side-effects. On the basis of the study results the need for postulation of a new definition of the term "neuroleptic" is indicated.

002622 Carlsson, C.; Dencker, S. J.; Grimby, G.; Haggendal, J.; Johnsson, G. Lillhagen Mental Hospital, Goteborg, Sweden **Hemodynamic effects of thiothixene and chlorpromazine in schizophrenic patients at rest and during exercise.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 13(4):262-268, 1976.

The hemodynamic effects and plasma levels of noradrenaline were studied in schizophrenic patients at rest and during exercise after long-term treatment with chlorpromazine and thiothixene. The results are compared with those from previous studies in untreated patients and patients receiving very large doses of chlorpromazine. The effects of thiothixene on the different hemodynamic variables were very moderate, and the observed differences between this group and the control group may be due to the different patient materials. In the two groups of patients receiving chlorpromazine, the heartrate at rest and during exercise tended to be higher than in the control group. There was also a tendency towards a lower stroke volume after this drug and thiothixene during exercise. The noradrenaline levels in plasma were highest after the high dose of chlorpromazine both at rest and during exercise, while they were lower after the moderate chlorpromazine dose. After thiothixene, the values were between those of the group on the low chlorpromazine dose and those of the control group. 13 references. (Author abstract)

002623 Chiu, Edmond; Burrows, Graham; Stevenson, James. Private Bag 3, P.O., Parkville, Victoria 3052, Australia **Double-blind comparison of clozapine with chlorpromazine in acute schizophrenic illness.** Australian and New Zealand Journal of Psychiatry (Carlton). 10(4):343-347, 1976.

A double-blind comparative trial of a new dibenzodiazepine derivative clozapine (Leponex) with chlorpromazine was conducted in the treatment of acute schizophrenic illness over a 6 week period. Factor analysis of ratings in nine matched pairs indicates that clozapine, at 300mg. per day, is comparable in efficacy to chlorpromazine in all factors except "irritability" for which clozapine appears to be superior. Illness severity and global change ratings in all patients showed that clozapine is more effective in producing a shift towards improvement at

the end of 6 weeks. Major side-effects reported in clozapine confirmed sedation and hypersalivation as consistent problems and presence of rigidity and tremor (extrapyramidal) being at variance with other studies. 7 references. (Author abstract)

002624 Crow, T. J.; Deakin, J. F. W.; Johnstone, E. C.; Longden, A. Clinical Research Centre, Northwick Park Hospital, Watford Road, Harrow, Middlesex HA1 3UJ, England **Dopamine and schizophrenia.** Lancet (London). No. 7993:1027, 1976.

In a letter to the editor, a criticism by Westerink and Korf of a previous communication is replied to. Attention is drawn to the differing selectivities of the neuroleptics on dopaminergic mechanisms in the nucleus accumbens and corpus striatum, and it is pointed out that for drugs of known therapeutic equivalence and differing extrapyramidal side-effects, the antipsychotic effects are closely paralleled by actions on dopaminergic mechanisms in the accumbens but not in the striatum. It is stated that ability to block the dopamine (DA) receptor, as assessed by blockade of the DA sensitive adenylate cyclase or by inhibition of haloperidol binding, appears to be the best predictor of therapeutic efficacy available. It is also stated that Westerink and Korf have not presented data which discount the DA blockade hypothesis of antipsychotic action because they have not demonstrated that there is a compound which can increase the concentration of DA metabolites in the nucleus accumbens by blocking DA receptors which has been shown to lack antipsychotic effectiveness. 7 references.

002625 Deniker, P. Centre Psychiatrique Saint-Anne, Paris, France **/Recent developments in the chemotherapy of schizophrenic psychoses./** Progres recents de la chimiotherapie des psychoses schizophreniques. In: Advances in the drug therapy of mental illness. Geneva, World Health Organization, 1976. 168 p. (p. 45-50).

Recent developments in the chemotherapy of schizophrenic psychoses are discussed. The need for more active research is emphasized, and the following areas are discussed: 1) nosological differences; 2) progress in the continuity of therapeutic action; 3) progress made in the classification and choice of therapeutic agents; and 4) gaps in therapeutic research. It is concluded that the governments have more or less abandoned therapeutic research to the sole initiative of the pharmaceutical companies. A call is made to the World Health Organization to support therapeutic research.

002626 Dia, A.; Boucly, J. Y. no address **/Use of Neuroleptic 19366 RP and its long-acting ester, the 19552 RP, on 19 patients at Hospital Center of Fann: Summary./** Emploi du Neuroleptique 19366 RP et son ester a longue duree d'action Le 19552 RP chez 19 malades au Centre Hospitalier de Fann -- Resume. African Journal of Psychiatry (Lagos). 2(1):245-246 1976.

In a paper presented at the Pan African Psychiatric Conference in Khartoum, Sudan, in November 1972, the therapeutic use of two narcoleptic drugs, 19366 RP (10 patients) and long acting 19552 RP (9 patients) in the management of psychotic hallucinatory and progressive delirium is summarized. Both agents were found effective as antihallucinogens. Side-effects were minor and responded to trihexiphenidyl (Artene). For best therapeutic results, it was suggested that treatment begin with 19366 RP 30mg t.i.d. for 1 month, followed by 19552 RP 50mg monthly for 3 months, decreased to 100mg every 6 months as needed.

002627 Eklund, Kurt L. Psyhiatric Clinic III, Sater Hospital, S-78300 Sater, Sweden **A double-blind comparison study between penfluridol and perphenazine in acute schizophrenic patients.** Nordisk Psykiatrisk Tidsskrift (Kungsbacka). 30(5):384-391, 1976.

Effects of penfluridol and perphenazine on 49 relapsed schizophrenic women, average age 46, were studied in a double-blind experiment. Periods of care and hospitalization for the women varied from 19 days to 21 years. Patients, taken off neuroleptics at least 3 days before the experiment, were treated for 2 weeks as inpatients with dosages of 24mg perphenazine daily and 100mg penfluridol weekly. Six ratings with the Brief Psychiatric Rating Scale (BPRS) and the Clinical Side Effect Scale were performed on the first 4 days and on days 8 and 15. Significant differences between the two groups occurred regarding conceptional disorganization, hallucinatory behavior, grandiosity, and unusual thought content and were more expressed in the perphenazine group. Penfluridol gave significantly more side-effects on days 2 and 3, though overall the same antipsychotic effect was obtained for both drugs. 8 references.

002628 Gamna, G.; Tavolaccini, L. Servizi Psichiatrici Provinciali del Settore di Torino-Est, Turin, Italy **/Use of a long-acting drug (pipotiazine palmitate) in hospital and outpatient therapy./** Impiego di un preparato "long-acting" (palmitato di pipotiazina) nell'esperienza ospedaliera ed extraospedaliera. Rivista Sperimentale di Freniatria (Reggio Emilia). 100(5):1239-1252, 1976.

The use of pipotiazine palmitate in 28 schizophrenics is evaluated, showing its long-acting quality, its effectiveness with outpatients and its propensity to enhance good rapport between therapist and patient. Patients were administered the drug for 4 to 32 months and then followed up for a period of 1 to 2 years with home visits and outpatient care. Best results were evidenced in paranoid schizophrenics, and hebephrenics showed the least amelioration. Results suggest that the drug's prolonged action is its most effective aspect. Other attractive factors include the small dosages in which the drug may be administered, and its feasibility for outpatient care. 15 references.

002629 Gillin, J. Christian; Kaplan, Jonathan A.; Wyatt, Richard Jed. Laboratory of Clinical Psychopharmacology, Division of Special Mental Health Research, St. Elizabeths Hospital, Washington, DC 20032 **Clinical effects of tryptophan in chronic schizophrenic patients.** Biological Psychiatry. 11(5):635-639, 1976.

L-tryptophan in high doses was administered to 8 male chronic undifferentiated schizophrenics in a double-blind format. It was found that L-tryptophan did not significantly affect overall ratings of psychosis, depression, anxiety, hallucinations or delusions. While results indicate that tryptophan administration neither improves nor exacerbates clinical conditions of most chronic male schizophrenics; however, there were individuals whose condition became better or worse during tryptophan administration. The addition of pyridoxine apparently did not alter the clinical effects of tryptophan. It is suggested that 5-hydroxytryptophan may not produce its beneficial effects by increasing serotonergic activity, and that further research is required to establish whether serotonin or abnormal metabolites of tryptophan are involved in the pathophysiology of schizophrenia. 26 references.

002630 Hese, Robert. Szpital Gorniczej, Oddzial Psychiatrycznej, Bytom, Poland **/Evaluation of atropine**

therapy in treating schizophrenia./ Wartosc atropinoterapii w leczeniu zespolow schizofrenicznych. Psychofarmakoterapia Schizofrenii Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 205-214).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs, in Schizophrenics held in Wroclaw, Poland, in October 1973, atropine therapy in treating schizophrenia is evaluated. All patients given atropine therapy had been subjected to unsuccessful neureleptic medication previously. The method employed was that of a combined atropine and neuroleptic treatment as developed in Gdansk. The results of atropine coma therapy indicate about 57% improvement in paranoid schizophrenia, whereas a 69% improvement was found in simple schizophrenia. A detailed tabulation of each patient's dosage, disease characteristics and treatment results are tabulated in the report. 18 references.

002631 Hirsch, S. R.; Usemann, Hans (translator). Charing Cross Hospital Medical School, Fulham Palace Road, London W. 6, England **/Care of schizophrenic patients outside the hospital: research results and basic principles./** Die Versorgung schizophrener Patienten ausserhalb des Krankenhauses: Forschungsergebnisse und Grundprinzipien. Nervenarzt (Berlin). 47(8):469-476, 1976.

Outpatient treatment of schizophrenics in England and Wales is dicuseed from the perspectives of care, rehabilitation, psychopharmacology, and prophylaxis. Schizophrenics are susceptible to primary, secondary, and premorbid handicaps, which affect functional skills to various degrees. The loss of social effectiveness can be attributed in part to understimulation or extended hospitalization. It has been found that rehabilitation must be gradual to prevent acute episodes triggered by sudden environmental changes. The relationship with the patient's person of reference after discharge is decisive in the catamnesis. Patients become accustomed to institutional shelter within 1 to 2 years. Chronic schizophrenics improve their industrial skills with time, but primary symptoms of agitation, exaggerated mannerisms and thinking aloud may also increase in intensity. It is suggested that patients with similar degrees of handicaps be placed together. Although phenothiazines are indicated for chronic patients, a large percentage of patients with short hospitalization recover spontaneously after the acute episode has ended. Double-blind tests have shown that patients under long-term oral medication have fewer relapses than untreated patients, especially when exposed to stress. 30 references.

002632 Jacobsson, L.; von Knorring, L.; Mattsson, B.; Mjorndal, T.; Oreland, L.; Perris, C.; Rapp W.; Edenius, ; Kettner, B. Department of Psychiatry, University of Umea, Umea, Sweden **Penfluridol and thiothixene: dosage, plasma levels and changes in psychopathology.** International Pharmacopsychiatry (Basel). 11(4):206-214, 1976.

The relationship between changes in plasma and dosage levels and changes in the psychopathology of 47 chronic schizophrenic patients given penfluridol or thiothixine was studied over a 4 week period. Double-blind trials showed a ten fold variation in plasma levels of penfluridol and a twenty fold variation for thiothixene with a significant correlation between plasma levels and changes in psychopathology as regards factor five in the Martens & Jonsson S-scale for both drugs. A significant correlation between dose and plasma level was found for penfluridol but could not be demonstrated for thiothixene. Gas chromatographic methods for determining the concentrations of major metabolites are described. 6 references. (Author abstract modified)

002633 Jankowska, Halina; Stanikowska, Izabela. I Klinika Psychiatryczna, Instytut Psychoneurologicznej, Warsaw, Poland **/Depression symptom scale for evaluating the success of neuroleptic treatment./** Skala objawow depresyjnych w ocenie wynikow leczenia neuroleptykami. Psychofarmakoterapia Schizofrenii Leki o Przedlyzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 115-116).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, a depression symptom scale is presented for measuring success of pharmacotherapy of schizophrenia. The scale is found to be applicable to schizophrenia studies giving results that are consistent with clinical evaluations. 6 references.

002634 Kai, Yasunobu. Kai Hospital, Tsukushi-cho, Yanagawa, Japan **The effect of L-dopa and vitamin B6 in schizophrenia.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 30(1):19-26, 1976.

A clinical trial is reported in which eight chronic schizophrenic inpatients who had previously failed to respond to low dose L-dopa therapy and conventional neuroleptics combined with low doses of vitamin B6, were treated with small doses of L-dopa and usual doses of vitamin B6. Improvement of psychotic symptoms was excellent in two cases, good in three cases, and fair in three cases, with no aggravated or unimproved cases. Both patients with durations of illness between 8 and 10 years were excellent responders whereas patients with durations of illness over 10 years were either moderately improved or not markedly improved. Normalization of EEG pattern preceded symptomatic amelioration in every case. 11 references.

002635 Kornetsky, Conan. Boston University School of Medicine, 80 E. Concord St., Boston, MA 02118 **Hyporesponsivity of chronic schizophrenic patients to dextroamphetamine.** Archives of General Psychiatry. 33(12):1425-1428, 1976.

A study of hyporesponsivity of chronic schizophrenics to dextroamphetamine is reported. Among the evidence supporting the dopamine hypothesis of schizophrenia is the finding that both amphetamine and methylphenidate hydrochloride, potent releasers of dopamine, can cause exacerbation of symptoms in the acute schizophrenic patient. Three experiments are described. In one experiment, orally administered, daily doses of 20mg of dextroamphetamine sulfate given at 8 PM had little or no effect on the sleep duration of the subjects. In the other two experiments, doses up to 40mg given orally also had little or no effect on the performance of the subjects on a variety of behavioral tests. There was no evidence of an exacerbation of the disease process in any of the subjects. The most consistent amphetamine effect was a dose related increase in blood pressure. These results indicate that the chronic schizophrenic patient may be hyporesponsive to amphetamine and suggest that if the dopamine hypothesis is correct, then it must be modified to take into account these findings in the chronic patient. 10 references. (Journal abstract)

002636 Lapierre, Y. D.; Lavallee, Jean. Pierre Jaffet Hospital, Hull, Quebec, Canada **A controlled pimozide, fluphenazine and group psychotherapy study of chronic schizophrenics.** Psychiatric Journal of the University of Ottawa (Ottawa). 1(1-2):8-13, 1976.

Thirty two chronic schizophrenic outpatients participated in a double-blind comparative study of pimozide and fluphenazine and an assessment of the value of combined

psychopharmacotherapy and brief group therapy. After 4 weeks of daily treatment, half the patients in both drug groups were assigned to weekly group psychotherapy. Assessment by the Brief Psychiatric Rating Scale (BPRS) and the Katz Social Adjustment Scale at onset and at 4, 8, 12, and 16 weeks showed that there was no real difference in global psychopathology for drug treatment or for psychotherapy. There was, however, a significant interaction exhibited between the two factors. The pimozide, fluphenazine and psychotherapy variables were associated with some statistically significant changes and differences in the clusters of thinking disorder and anergia. Assessment of the psychotherapy participation demonstrated that the patients on pimozide tended to have a lesser quantity of speech and that their speech was more adequate. They had a significantly more adequate affective involvement and more adequate integration to the group. There were no drug differences on the variables of attendance, dress, and body language. 7 references. (Author abstract modified)

002637 Lavagna, J.; Lafont, A.; Darcourt, G. Service de Psychiatrie et de Psychologie Medicale, Hopital Pasteur, F-06035 Nice Cedex, France **/Use of haloperidol at very high dosage./** Utilisation de l'haloperidol a de tres fortes doses. Encephale (Paris). 2(4):363-365, 1976.

Use of haloperidol in very high doses is reported. A group of 12 patients, 7 females and 5 males, 17 to 53 years old, presenting severe paranoid reaction with excitement and including nine schizophrenics, was given 60mg haloperidol p.o. for periods of 15 to 106 days. This treatment was insufficient to calm the agitation and necessitated an increase in dosage in one case and administration with another neuroleptic in the remaining cases. Tolerance was good in all cases. It is suggested that because of its good tolerance haloperidol in high doses is advisable for very acute cases of delirious agitation.

002638 Lecomte, G. Psychiatre des Hopitaux, Marseilles, France **/The psychiatric sector and the walls of the asylum./** Le secteur et les murs de l'asile. Encephale (Paris). 2(3):229-230, 1976.

A case report of a female patient with a chronic delusion was presented at the 10es Journees d'Information Psychiatrique, Marseilles, 1976. The patient was successfully treated with an injection of 25 mg Piportil L4 every 6 weeks, which abolished the delusion and allowed her to live a normal life without hospitalization and its stigmatization.

002639 Leff, J. P. M.R.C. Social Psychiatry Unit, Institute of Psychiatry, London, England **The maintenance and management of schizophrenia.** Irish Medical Journal (Dublin). 69(17):464-468, 1976.

A study of the maintenance and management of schizophrenic patients in the community is presented. Patients with good premorbid personality experiencing a first attack of schizophrenia with an acute onset and marked depressive symptoms in addition to typical schizophrenic symptoms can often do well without maintenance pharmacotherapy. Patients who tend to stop modification of their own accord after being discharged from the hospital might do well if they were treated with long-acting injections. Life events may act as triggers of relapses. Patients living with a relative who had a high index of expressed emotion relapsed more than patients whose relative had a low index of expressed emotion. In the former situation, social distance from their relative and maintenance phenothiazine therapy aided the patient's survival. It is suggested that therapist aim at increasing the social distance between the relative and the patient. 12 references.

002640 Levinson, A. Ya. Tadzhikskiy meditsinskiy institut, Dyushambe, USSR **/Formation of circularity as a manifestation of pathomorphosis in schizophrenia./** Vozniknoveniye tsirkulyarnosti kak proyavleniye patomorfoza shizofrenii. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova (Moskva). 76(12):1843-1847, 1976.

Circularity in schizophrenia was examined on the assumption that it cannot be explained solely as an outcome of the use of psychotropic drugs. The origin of cyclothymic behavior is considered on the basis of fundamental and secondary psychopathological factors in the establishment of clinical symptoms of psychoses. Three categories of schizophrenia are considered: 1) disorders in vital affective registers which occur only in late stages of the disease; 2) process of the disease outside the framework of circularity resulting from clinically developing factors; 3) extended periods of remission between attacks. It is concluded that circularity is not a central cause of schizophrenia and that psychotropic agents are not a prime factor. 15 references.

002641 MacKay, A. V. P. Department of Psychological Medicine, Royal Edinburgh Hospital, Edinburgh, Scotland **The measurement of plasma chlorpromazine and its metabolites as a predictor of response in chronic schizophrenics.** In: Advances in the drug therapy of mental illness. Geneva, World Health Organization, 1976. 168 p. (p. 122-126).

The relationship of chlorpromazine and its sulfoxy and 7-hydroxy metabolites to oral dose and global control of symptoms was studied in a large inpatient population of chronic schizophrenics. A tenuous relationship between the plasma concentration of chlorpromazine and clinical response was found during the first two weeks of drug treatment. This response pattern disappeared over longer periods of time. The results emphasize the unpredictability of the relationship between oral dosage and plasma concentrations of chlorpromazine and its metabolites. It is concluded that the lack of correlation between clinical state and plasma concentration of unchanged drug indicates that a more accurate prediction of therapeutic response should be developed. 11 references.

002642 Malik, Kazimierz; Wroblewska, Janina; Zygala, Pawel. Wojewodzkiej Szpital dla Nerwowo i Psychicznie Chorych, Jaroslaw, Poland **/Treatment of schizophrenia and schizophrenic psychosis at Jaroslaw Hospital in 1972./** Leczenie schizofrenii i psychoz shizofrenicznych w szpitalu w jaroslawiu w 1972 roku. Psychofarmakoterapia Schizofrenii Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 155-160).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, of schizophrenia and schizophrenic psychoses at Jaroslaw Hospital is reviewed for 1972. All patients suffering from schizophrenia for which diagnosis was positive and who were released in 1972 formed the data group. Data for neuroleptic, multiple neuroleptic, neuroleptic plus ECT, neuroleptic plus insulin shock, and other therapeutic methods are given, together with results. No conclusions are drawn as this study is preliminary to a future followup on the released patients.

002643 Marcjan, Kazimierz; Pietruszewska, Irena; Wolak, Ewa. Klinika Psychiatryczna, Akademia Medyczna, Warsaw, Poland **/Five years of experience with prolonged action fluphenazine./** Piec lat doswiadczen z flufenazyna o przedluzonym dzialaniu. Psychofarmakoterapia Schizofrenii Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 103-110).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, 5 years' experience with prolonged action fluphenazine is described and analyzed. The drug was administered to 143 schizophrenics with various degrees of severity and duration of the disease. Effectivenss was evaluated on a six point scale as a function of disease duration, and side-effects were tabulated. The study indicates that fluphenazine is a strong neuroleptic in newly established as well as chronic schizophrenia. The drug exhibits low toxicity, but it does have extrapyramidal side-effects and psychotic effects. 15 references.

002644 Marriott, Peter; Hiep, Albert. Private Bag 3, Parkville, Vic., 3052, Australia **A mirror image out-patient study at a depot phenothiazine clinic.** Australian and New Zealand Journal of Psychiatry (Carlton). 10(2):163-167, 1976.

A mirror image study at a specialized outpatient clinic for the long-term management of psychiatric disorders is presented. A mirror image study is described as one in which pretherapy hospital stay duration is compared to hospital stay duration after therapy is commenced with the subjects acting as their own controls. The subjects were 131 schizophrenic patients to be treated with phenothiazine. Results showed that 95 of the patients had diminished hospitalization periods after therapy was instituted. It was concluded that regular taking of medication, in this instance phenothiazine, is a crucial factor leading to improvement in schizophrenic patients. 15 references.

002645 Masiak, Marek; Majczak, Adam; Hascewicz-Rzecka, Maria; Kowalczyk, Anna. Klinika Psychiatryczna Instytutu Chorob Uklady Nerwowego AM, il. Abramowicka 2, 20-442, Lublin, Poland **/Clinical evaluation of pimozide and piportil in treatment of chronic schizophrenia./** Badania nad zastosowaniem pimozidu i piportilu w leczeniu chorych na przewlekla schizofrenie. (Doniesienie wstepne). Psychiatria Polska (Warszawa). 10(6):655-660, 1976.

Clinical evaluation of pimozide and piportil was made in the treatment of chronic schizophrenia, based on comparison of 15 patients receiving pimozide and 14 patients receiving piportil in a double-blind study. Clinical and behavioral scales were used to assess changes in patients' mental condition. Results indicate that positive therapeutic changes were obtained with pimozide in patients with predominantly delusional hallucinatory symptoms and also in patients with activity impairment, while piportil acted best in patients with schizoaffective psychosis and in cases with certain forms of paranoid schizophrenia. 14 references. (Journal abstract modified)

002646 McClelland, Hamish A.; Farquharson, Robin G.; Leyburn, Peter; Furness, John A.; Schiff, Anthony A. St. Nicholas Hospital, Gosforth, Newcastle upon Tyne NE3 3XT, England **Very high dose fluphenazine decanoate.** Archives of General Psychiatry. 33(12):1435-1439, 1976.

In a double-blind trial of 6 months' duration, a very high dose (VHD) regimen of fluphenazine decanoate (250mg weekly) was compared with a standard dose (SD) regimen (12.5mg weekly) in 50 chronic schizophrenic patients. The rating scales used included the Brief Psychiatric Rating Scale and the Wind Ward Behavior Scale. Both treatment groups improved during the trial, but there was no significant difference between them. The VHD regimen, however, exerted better control of the psychosis in that it had fewer patient dropouts and fewer additional treatments prescribed. Some of the patients receiving standard doses were probably not receiving adequate antipsychotic drug dosage. No predictors of clinical response could be defined. Extrapyramidal side-effects were not significantly higher in the VHD group. 8 references. (Journal abstract)

002647 Nahunek, K.; Svestka, J.; Rodova, A.; Misurec, J.; Vyborova, L. Psychiatricka Klinika LF UJEP, Brno, Czechoslovakia **/Results of clinical and experimental testing of Czechoslovak neuroleptics octoclothepin and oxyprothepin./** Vysledky klinickeho a experimentalniho zkouseni cs. neuroleptik octoclothepinu a oxyprothepinu. Ceskoslovenska Psychiatrie (Praha). 72(1):32-40, 1976.

Experience with octoclothepin and oxyprothepin treatment in 5 controlled double-blind crossover trials is summarized and a number of open clinical and experimental studies are described. Both neuroleptics tested were found to have a high milligram effectiveness as well as a high affinity for both the extrapyramidal and vegetative nervous systems with a discernible element of sedative hypnotic effect particularly in the first days of treatment. In dosages of up to 15mg daily, which appeared sufficiently effective in most of the patients, these side effects were cut down to a reasonable acceptable degree. The two neuroleptics were found to be extremely effective antimanic drugs. In the schizophrenia group the effect was found to be more favorable in the productive forms of the disease with the noninhibitory effect being less pronounced. In the endogenous depression group successful impact was made particularly on some of the atypical forms with paranoid/hallucinatory, schizoform, and amentiform components. Psychomotor instability syndrome in children was in most cases favourably affected with a quick onset of the effect. Oxyprothepin proved to have a more profound effect on cardiovascular functions. Octoclothepin showed a higher inhibitory effect on awareness, visuomotor coordination, motor performance, and electroencephalogram. 32 references. (Journal abstract modified)

002648 Nair, N. P. V.; Decker, B. L.; Schwartz, G. Research Department, Douglas Hospital Centre, 6875 LaSalle Blvd., Montreal, Quebec, Canada **Loxapine succinate in the treatment of chronic schizophrenia.** Current Therapeutic Research. 20(6):802-809, 1976.

The therapeutic efficacy, target symptom specificity and adverse effects of loxapine succinate were evaluated in a 12 week uncontrolled clinical trial with 10 schizophrenic patients. The results generally confirm that loxapine, in 90 to 150mg/day dosage, is an effective antipsychotic. It was particularly active on such symptoms as aggressiveness, irritability, and uncooperativeness. This study utilized the newly revised factors of the Brief Psychiatric Rating Scale (BPRS) and comparisons with other studies are made. 12 references. (Author abstract)

002649 Noonan, J. P. A.; Burnstein, M. H.; Ananth, J.; Clark R. St. Mary's Hospital, 3830 Lacombe Avenue, Montreal, P. Q., Canada **Sex and neuroleptic medication.** Psychiatric Journal of the University of Ottawa (Ottawa). 1(1-2):86-87, 1976.

A possible differential response to neuroleptic drugs between male and female patients was investigated in 114 chronic schizophrenic patients. The dosage of medication received per pound bodyweight was determined. There was a statistically significant difference in the daily dosage of medication expressed in chlorpromazine units between male and female patients below 50 years old. No significant difference was observed in patients over 50 years old or in the total population. The finding that premenopausal females need more

medication than males of similar age points to the possibility that sex itself is the differentiating factor and that differences are related to androgen levels. 4 references. (Author abstract modified)

002650 Nurowska, Krystyna; Welbel, Leszek. Instytut Psychoneurologicznej, Warsaw, Poland /**Comparative evaluation of maintenance treatment in chronic schizophrenia using fluphenazine and flupenthixol in slow-release form.**/ Porownawcza ocena leczenia podtrzymujacego w przewleklej schizofrenii przy uzyciu flufenazyny i flupentiksolu o przedluzonym dzialaniu. Psychofarmakoterapia Schizofrenni Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 127-131).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, a comparative evaluation of maintenance treatments in chronic schizophrenia using fluphenazine and flupenthixol in slow release form, administered to two groups of patients is presented. One group received prolonged action fluphenazine and the other group received flupenthixol depot. Concurrently, two smaller groups received conventional forms of the same drugs. All patients had initially been treated in the conventional manner and were subsequently placed on a maintenance dosage. Results show favorable action of the prolonged action drugs, and although results of the two types of drugs are similar, somewhat better results were obtained with fluphenazine.

002651 Olesinski, Zygmunt; Trembla, Krzysztof. Wojewodzkiej Szpital Chorob Ukladu Nerwowego, Lubiaz, Poland /**Comparative evaluation of moditen depot and conventional maintenance treatment using neuroleptics.**/ Porownawcza ocena stosowania moditenu-depot i tradycyjnego leczenia podtrzymujacego neuroleptykami. Psychofarmakoterapia Schizofrenii Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 143-147).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, a comparative evaluation was made of moditen depot and traditional neuroleptic maintenance treatment. The patients treated all exhibited psychotic relapse when their normal dosages were reduced. Applications of moditen depot, however, resulted in significant improvement of the patients' psychic state.

002652 Ratel, M.; Boucharlat, J.; Maitre, A.; Wolf, R.; Ledru, J. no address /**Acute catatonias with favorable outcome: a report of two cases.**/ Catatonies aigues a evolution favorable. A propos de deux cas. Annales Medico-Psychologiques (Paris). 1(2):230-237, 1976.

Two cases of acute catatonia were reported at a meeting of the Societe Medico-Psychologique on January 26, 1976. One was a 40-year-old female, and the other a 24-year-old male. Both patients showed the mute form of catatonia. They were treated with doxepine, followed by electroshock therapy. The first patient required subsequent treatment with Anafranil, Nozinan, and Lithium, while the second patient could be discharged without subsequent pharmacotherapy. Hospitalization lasted 3 1/2 months for the first patient and 1 1/2 months for the second patient. The management of electrolyte and fluid balance in catatonia is discussed. 18 references.

002653 Simon, P.; Ginestet, D. Departement de Pharmacologie U 5 Paris, Frances /**Methodological problems of a comparative study of prolonged action neuroleptics and classical neuroleptics.**/ Les problemes methodologiques d'une etude comparee de neuroleptiques d'action prolongee et neuroleptiques classiques. Psychologie Medicale (Paris). 8(8):1233-1242, 1976.

Group discussion on methodological problems of a study comparing prolonged action neuroleptics with classical neuroleptics at the 4th Methodology of Research in Psychiatry Meeting, held in Marseille, April 1975, covered the experience of a team research project. The study was conducted over a 20 month period by 30 psychiatrists, who worked in 14 centers with 74 schizophrenic patients. Personal differences between team members raised difficulties in cooperation, but also pointed up the necessity for a joint effort in comparing the two types of neuroleptics.

002654 Singh, Man Mohan; Kay, Stanley R. Clinical Psychopharmacology Unit, Bronx Psychiatric Center, 1500 Waters Place, Bronx, NY 10461 **Cholinergic processes in schizophrenia.** World Journal of Psychosynthesis. 8(5):34-41, 1976.

To determine possible therapeutic antagonism between antiparkinsonism (AP) agents and neuroleptics in the treatment of schizophrenia, a series of nonblind and double-blind studies are reviewed in which schizophrenic inpatients were administered: haloperidol and benztropine, haloperidol and trihexyphenidyl, haloperidol/chlorpromazine and benztropine, and haloperidol/chlorpromazine and trihexyphenidyl. Overall data indicate that anticholinergic AP agents have countertherapeutic effects when combined with neuroleptics, and that they exacerbate psychosis when given alone. The findings, especially when considered in relation to treatment responsiveness, suggest a direct therapeutic antagonism between anticholinergics and neuroleptics in schizophrenia and point to the possibility that built in anticholinergic properties may be one of the determining factors in the lower potency of antipsychotic drugs such as chlorpromazine. The possibility of anticholinergic/neuroleptic antagonism is also supported by animal data which show that anticholinergics reverse behavioral pharmacological effects predictive of antipsychotic activity. 35 references. (Author abstract modified)

002655 Skaryszewska-Sawicka, Jadwiga; Szemis, Andrzej; Pasterski, Jerzy; Wlosinska, Irena. Klinika Psychiatryczna, Akademia Medyczna, Warsaw, Poland /**Clinical evaluation of flupenthixol with prolonged action.**/ Ocena kliniczna flupentiksolu o przedluzonym dzialaniu. Psychofarmakoterapia Schizofrenii Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 121-125).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, the effectiveness of prolonged action flupenthixol was clinically evaluated in outpatients. On the basis of study of 46 patients, it is concluded that flupenthixol is a valuable drug for outpatient use, especially in patients with chronic schizophrenia. The drug is particularly effective for schizophrenics with subsiding symptoms, but it is not indicated for patients with psychomotor disturbances. Because of side-effects it is necessary to maintain continuous supervision and caution is recommended in drug application. 11 references.

002656 Suarez Richards, Manuel; Zelaschi, Norberto Mario; Canero, Ernesto. Hospital A. Korn, de Melchor Romero, Pcia. de Buenos Aires, Argentina /**A new neuroleptic for long-term therapy: penfluridol (R-16341).**/ Actividad de un nuevo neuroleptico, penfluridol (R-16341) en tratamientos de larga dura-

cion. Acta Psiquiatrica y Psicologica de America Latina (Buenos Aires). 22(3):205-210, 1976.

The results of long-term therapy with penfluridol (R-16341), a neuroleptic drug, are presented. Penfluridol was administered to 26 female schizophrenic subjects (20 inpatients and 6 outpatients), ages 17 to 54 years. The patients were divided into two groups of 13, and were given one weekly oral dose of between 10 and 100 mg over a 90 day period. The first group added this drug to prescriptions already in use. The second group gradually discontinued all other medication. The results were evaluated according to 36 factors. The side-effects were few and temporary, including insomnia in 7 cases during the first week and extrapyramidal symptoms in another 7 cases which was controlled with antiparkinsonians. It was concluded that penfluridol was a useful and effective neuroleptic drug for managing schizophrenic patients. 10 references. (Journal abstract modified)

002657 Vencovsky, E.; Peterova, E.; Baudis, P. Psychiatricka klinika LF KU, Plzen, Czechoslovakia **/On the problem of side-effects of clozapine./** K otazce vedlejsich ucinku clozapinu. Ceskoslovenska Psychiatrie (Praha). 72(1):4-6, 1976.

Clinical experience provides unambiguous proof of clozapin (Leponex "Sandoz") being an excellent neuroleptic, the antipsychotic effect of which is brought on relatively early, stabilizing symptoms while maintaining the compensation of the psychotic state under a low dose treatment. Another advantage is that there are extremely few concomitant extrapyrimidal signs, particularly concerning paroxysmal dyskinesis. Negative aspects include the incidence of vegetative side effects, though not necessarily of any high intensity, which appear to be more frequent than in the case of other neuroleptics. (Journal abstract modified)

002658 Villeneuve, C.; Jus, K. Division des Recherches, Hopital St. Michel-Archange, Quebec 5, Canada **/Intermittent psychopharmacotherapy: review of literature and critical remarks./** Therapie intermittente en psychopharmacologie: revue de la litterature et remarques critiques. Vie Medicale au Canada Francais (Quebec). 5(9):940, 952-957, 1976.

A review of the literature on intermittant psychopharmacotherapy reveals short-term intermittent psychopharmacotherapy based on drug free intervals of 3 days per week, seems to be a safe and adequate method of reducing the initial maintenance dosage in well stabilized chronic schizophrenic patients on a stable maintenance dosage. There are several benefits for the patient as well as for the nursing personnel and drug expenses can be converted into other useful services for patients. On the other hand, long-term intermittent psychopharmacotherapy based on intervals of several months requires great caution in the selection of schizophrenic patients, taking into account especially the duration of hospitalization and the dosage of neuroleptics. In any case, the drug free intervals should not exceed 2 to 3 months for the majority of patients. 28 references. (Journal abstract)

002659 Wasik, August; Horodnicki, Jan; Brys, Jozef; Sidorowicz, Wladyslaw. Klinika Psychiatryczna, Akademia Medyczna, Wroclaw, Poland **/Initial clinical evaluation of moditen-depot./** Wstepna ocena kliniczna preparatu moditen-depot. Psychofarmakoterapia Schizofrenii Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 161-164).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, an initial clinical evaluation of moditen depot indicating good neuroleptic action similar to oral fluphenazine is presented. It is a convenient drug for patients who are negatively inclined to the treatment process. During the treatment, extrapyramidal disturbances are frequent, requiring corrective measures. Drug tolerance is evaluated as good. 6 references.

002660 Wodka, Ludwik. Panstwowej Szpital dla Nerwowo i psychicznie Chorych im Dr. E. Cyrana, Lublin, Poland **/Results of moditen-depot treatment in chronic schizophrenia./** Wyniki leczenia przewleklej schizofrenii moditenem-depot. Psychofarmakoterapia Schizofrenii Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 133-135).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, results of moditen depot treatment in chronic schizophrenia are presented. In a group of 25 patients, 9 showed good response, 7 satisfactory response, 5 showed adverse reaction. Side-effects were either slight or easily controllable.

002661 Wojdyslawska, Irena. Klinika Psychiatryczna AM, 159 Aleksandrowska ul., Lodz, Poland **/Treatments of schizophrenia with triflupromazine depot./** Leczenie schizofrenii trifluoroperazyna o przedluzonym dzialaniu. Psychiatria Polska (Warszawa). 10(6):703-704, 1976.

A study of treatment of schizophrenia with triflupromazine depot is presented, based on experience with a group of 25 patients, (18 females, 7 males) aged 18 to 54 years, who previously had been treated with various neuroleptics, ECT and insulin shock. Triflupromazine treatment had very good results in 16 patients, of whom seven showed complete remission of psychotic symptoms, nine showed significant improvement, five had some improvement, and four were withdrawn from the treatment because of lack of improvement. Results indicate that the tolerance of triflupromazine is good, it is easy to use, and that it is a significant drug in the treatment of schizophrenia.

002662 Wojdyslawska, Irena; Goraj, Andrzej; Soczynska, Joanna. Klinika Psychiatryczna AM, ul. Aleksandrowska 159, 91 299 Lodz, Poland **/Clinical evaluation of clozapine: a follow-up study./** Ocena kliniczna klozapiny z uwzglednieniem badan katamnestycznych. Psychiatria Polska (Warszawa). 10(5):497-502, 1976.

A followup study of clinical pharmacotherapy with clozapine is presented, based on 71 patients, 65 of whom were diagnosed as schizophrenics. Clozapine treatment at the clinic lasted on the average 60 days, after which the drug was given on an outpatient basis, and the followup period ranged from 1.5to 2.5years. Results of the followup study revealed that lasting remission of 1.5to 2.5years was obtained in 33 cases (68%), and good therapeutic effects were noted most often in psychosis with high psychopathological production and behavioral changes. On the maintenance dosage level tolerance was good, side-effects were minimal, allowing for personal and social activity. 9 references. (Journal abstract modified)

002663 Yorkston, Neil J.; Zaki, S. A.; Themen, J. F. A.; Havard, C. W. H. Friern Hospital, London, England **Propranolol to control schizophrenic symptoms: 55 patients.** In: Carlsson, C., Neuro-psychiatric effects of adrenergic beta-receptor. Munich, Urban & Schwarzenburg, 1976. 120 p. (p. 91-104).

In a paper presented to a symposium on neuropsychiatric effects of adrenergic beta-receptor blocking agents held at Copenhagen, October 1975, the results of a trial of propranolol as a control of symptoms in 55 schizophrenic patients are reported. Florid schizophrenic symptoms were found to remit at least temporarily in 28 of the 55 adults. Whereas 17 remitted on propranolol alone, 11 others required the addition of a phenothiazine drug. Individuals whose symptoms remitted felt and looked well, and their scores on a modified Brief Psychiatric Rating Scale fell to zero. It was found that careful monitoring was necessary to avoid acute toxic effects, which were severe in 5 cases when the dose was raised rapidly; moderate or mild toxic effects were seen in 32 cases, whereas 18 showed none. The dose of propranolol at remission ranged from 160 to 3000mg per day. The maintainance dose ranged between 160 and 2000mg per day. Remission usually was gradual and progressive, but sometimes was sudden; the time range for remission was from 72 hours to 12 months. It was found that progress was often irregular when the dosage was irregular. 12 references. (Author abstract modified)

002664 Zyg, Jan; Krol, Krystyna; Krystof, Jan; Skoczkowski, Jacek. Wojewodzkiej Szpital Chorob Ukladu Nerwowego, Boleslaw, Poland **/Clinical evaluation of moditen-depot and thioridazine-prolongatum in treatment of schizophrenia./** Kliniczna ocena dzialania moditen-depot i thioridazin-prolongatum w leczeniu przewleklej schizophrenii. Psychofarmakoterapia Schizofreni Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 137-141).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, a clinical evaluation of moditen depot and thioridazine prolongatum treatment of schizophrenia is presented. Results are based on studies of two separate groups and indicate that both the prolonged action neuroleptics represent a significant advance in schizophrenia treatment for both inpatients and outpatients. Caution is recommended, however, because of individual reactions, possible side-effects and the problem of arresting the effect of the drugs once it has been given. 27 references.

09 DRUG TRIALS IN AFFECTIVE DISORDERS

002665 Baastrup, Poul C.; Hollnagel, Peter; Sorensen, Rudulf; Schou, Mogens. Psychiatric Hospital, Glostrup, Denmark **Adverse reactions in treatment with lithium carbonate and haloperidol.** Journal of the American Medical Association. 236(23):2645-2646, 1976.

Reactions of 425 patients treated simultaneously with lithium carbonate and haloperidol were compared to those of patients given lithium alone or haloperidol alone. Of the 425 patients, a diagnosis of bipolar type manic-depressive disorder was made in 417 cases and schizoaffective disorder in eight. Treatment with lithium and haloperidol led to side-effects of the types seen during treatment with lithium alone and haloperidol alone; combination of the two drugs did not appear to increase either the frequency or the intensity of side-effects. None of the patients treated with the combination developed a syndrome of neuromuscular symptoms, impairment of consciousness, hyperthermia, and permanent neurological sequelae such as reported by Cohen and Cohen in 1974. It is concluded that the combination of lithium and haloperidol is therapeutically useful when administered to the diagnostically appropriate patients. 4 references. (Author abstract modified)

002666 Bertilsson, Leif; Asberg, Marie. Department of Clinical Pharmacology, Huddinge Hospital, S-14186 Huddinge, Sweden **Determination of biogenic amine metabolites in cerebrospinal fluid by mass fragmentography -- methods and biochemical studies of depressive disorders.** In: Airaksinen, M., CNS and behavioural pharmacology. Elmsford, New York, Pergamon Press, 1976. 344 p. v. 3. (p. 269-276).

In a paper presented at the Sixth International Congress of Pharmacology held in Helsinki, Finland in July, 1975, mass fragmentographic methods for the determination of amine metabolites in cerebrospinal fluid (CSF) are reviewed and studies of the levels of amine metabolites in the CSF of depressed patients before and after antidepressant therapy are reported. Methods are discussed for the quantitation in CSF of: 1) 5-hydroxyindoleacetic acid (5-HIAA); 2) indoleacetic acid; 3) homovanillic acid (HVA); 4) isohomovanillic acid; 5) 3-methoxy-4-hydroxyphenylglycol (MHPG); and 6) vanillylmandelic acid (VMA). Studies of pretreatment levels of 5-HIAA in the CSF of depressed patients have revealed a bimodal distribution of 5-HIAA, suggesting that depression, especially the endogenous type, may be a biochemically heterogeneous disease. It has been hypothesized that patients with a low 5-HIAA level in CSF may have a disturbed serotonin (5-hydroxytryptamine, 5-HT) metabolism, while those with higher levels of 5-HIAA may have other metabolic disturbances, possibly of noradrenalin (NA) metabolism. Clinical studies have indicated that: 1) patients with high CSF 5-HIAA levels are more responsive to nortriptyline, which is a potent inhibitor of NA uptake with little effect on 5-HT uptake, than are patients with low CSF 5-HIAA levels; 2) MHPG levels in CSF are significantly decreased during treatment with either chlorimipramine or nortriptyline; 3) 5-HIAA levels are significantly decreased during chlorimipramine treatment, but not during nortriptyline treatment; and 4) during chlorimipramine treatment, 5-HIAA levels are decreased more than are MHPG levels and HVA levels are slightly increased but the increase is not statistically significant. It is concluded that the measurement of amine metabolites in CSF seems to be a useful tool for studies of the biochemical profiles of psychotropic drugs in humans. 19 references.

002667 Bielski, Robert J.; Friedel, Robert O. Dept. of Psychiatry, Michigan State University, East Lansing, MI **Prediction of tricyclic antidepressant response: a critical review.** Archives of General Psychiatry. 33(12):1479-1489, 1976.

Prospective, double-blind controlled studies that have evaluated the prediction of response to imipramine hydrochloride and amitriptyline hydrochloride in depressed patients are reviewed. Despite widely divergent methodologies, an attempt is made to extract clinically useful conclusions from these data. Critiques of each study and the criteria used in their evaluation are presented, with suggestions for future research included. The predictors of positive response to imipramine and amitriptyline are as follows: upper socioeconomic class, insiduous onset, anorexia, weight loss, middle and late insomnia, and psychomotor disturbance. The predictors of poor response are the following: neurotic, hypochondriacal, and hysterical traits, multiple prior episodes, and delusions. Pretreatment urinary 3-methoxy-4-hydroxyhenylglycol levels may some day be useful in predicting to which of these two tricyclic antidepressants a patient will respond. 87 references. (Journal abstract)

002668 Brion, S.; Chevalier, J. F.; Guerin, R.; Ginestet, D. Service de Psychiatrie Adultes, Centre Hospitalier de Versailles, 1, rue Richaud, F-78000 Versailles, France

/Chemotherapy of melancholia by sequential association of a neuroleptic and viloxazine./ Chimiotherapie de la melancolie par l'association sequentielle neuroleptique-viloxazine. Encephale (Paris). 2(3):257-271, 1976.

The combination of a tranquilizer followed by viloxazine was studied in 10 depressed patients. Viloxazine when used alone can cause an aggravation of anxiety and agitation or manic states. Therapy was started with one of the following: 3 to 10mg/day haloperidol, 100 to 150mg/day levomepromazine, 150 to 200mg/day chlorpromazine, or 200mg i.m. sulpiride. After 3 to 10 days, viloxazine was added in a dose of 150 to 300mg/day and the major tranquilizer was continued for several days. Diagnoses of the patients were manic depressive psychosis in three, endogenous depression in two, reactive depression in three, limited state in one, and psychotic depression in one. Very good results were obtained in the three manic-depressives and good results in two of the three reactive depressives. For the remaining patients, results were fair or null. Case reports are given for 14 patients treated with viloxazine, the first 2 of whom received viloxazine alone. 3 references.

002669 Bukowczyk, Adam; Wasik, August; Brys, Jozef; Michalska, Malgorzata; Fiszer, Teresa; Sidorowicz, Slawomir; Firko, Marek. Klinika Psychiatryczna, Akademia Medyczna, Wroclaw, Poland **/Treatment of depression with Ludiomil Ciba./** Ludiomil Ciba w leczeniu stanow depresyjnych. Psychofarmakoterapia Schizofrenii Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 173-175).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, Ludiomil, a Ciba drug, is discussed for treatment of depression. The data and observations of the manufacturer are summarized and original clinical data on 18 patients are included. The drug is found to be effective and can be used for patients with suicidal traits. 5 references.

002670 Condini, A.; Vizziello, G. Fava. Clinica delle Malattie Nervose e Mentali dell'Universita di Padova, Padua, Italy **/Psychodynamic observations of a group of patients treated with lithium carbonate./** Rilievi psicodinamici in pazienti trattati con litio. Rivista di Patologia Nervosa e Mentale (Firenze). 97(1):1-6, 1976.

The use of lithium carbonate with 45 cyclothymic patients over a 3 year period is evaluated to show how effective the drug can be with manic-depressives and how the patient behaves in relation to the drug and the therapist. Patients were checked monthly to insure that the lithiemia level was constant. Patients were also observed at this time for overall behavior. After 3 years, conclusive results showed that patient behavior was more controlled, lithium carbonate was well tolerated, and that the patient developed a dependence upon the drug rather than upon the therapist. Consequently, a better communicative relationship with the therapist ensues, as was shown in 90% of the patients. 8 references.

002671 Gabriel, E.; Kufferle, B.; Lenz, G.; Schuster, P. Psychiatrische Universitatsklinik, Lazarettgasse 14, A-1090, Wien, Austria **/On the conditions underlying particular pharmacogenic confusional states: a comparison of amitriptyline and clozapine./** Uber die individuellen Bedingungen pharmakogener Verwirrtheiten: Ein Vergleich zwischen Amitriptylin- und Clozapinkuren. Psychiatria Clinica (Basel). 9(1):5-13, 1976.

Discrepancies in the literature concerning the frequency and conditions for confusional states and deliria following amitriptyline and clozapine treatment are discussed and a retrospective investigation of such effects in a group of patients treated with amitriptyline and clozapine is reported. Experience with amitriptyline was similar to that of other investigators. With clozapine, however, confusional states and deliria were four times as frequent as the average reported in the literature. It is noted that the latter depend on conditions different from those of confusional states and deliria due to amitriptyline. There was a slightly significant correlation between the appearance of confusion and a temperature of over 37.5degrees C. The anticholinergic properties of amitriptyline and clozapine cannot explain the difference in frequency, nor the differing conditions for the appearance, of pharmacogenic confusional states and deliria with the two substances. 26 references. (Author abstract modified)

002672 Garfinkel, Paul E.; Warsh, Jerry J.; Stancer, Harvey C.; Sibony, David. Department of Psychiatry, University of Toronto, Clarke Institute of Psychiatry, Toronto, Canada **Total and free plasma tryptophan levels in patients with affective disorders: effects of a peripheral decarboxylase inhibitor, MST 1R8** Archives of General Psychiatry. 33(12):1462-1466, 1976.

Total and free plasma tryptophan levels in patients with affective disorders were studied. Previous reports of decreased cerebrospinal fluid tryptophan levels and decreased free plasma tryptophan levels, as well as a reduction in the volume of distribution of trytophan may occur in depressives. The disposition of plasma tryptophan was tested in 10 normal controls and 10 depressed patients. These measures were made on 2 drug free baseline days and on 2 days when the subjects had been receiving the peripheral decarboxylase inhibitor, carbidopa, which inhibits tryptophan metabolism via extracerebral indoleamine pathways. During the baseline days no statistically significant differences were found between the patients and controls in either total or free plasma tryptophan levels. For controls, there was no change in total tryptophan, but a significant decrease occurred in free plasma tryptophan concentrations while receiving carbidopa. In patients, the perturbing effects of carbidopa resulted in an increase in both total and free plasma tryptophan levels. These results suggest that an altered flux of tryptophan metabolism may exist in depressed patients that is uncovered by the administration of an extracerebral decarboxylase inhibitor. 65 references. (Journal abstract)

002673 Gerner, Robert H.; Post, Robert M.; Bunney, William E., Jr. Dept. of Psychiatry, University of California, Los Angeles School of Medicine, Los Angeles, CA **A dopaminergic mechanism in mania.** American Journal of Psychiatry. 133(10):1177-1180, 1976.

A case of a 47-year-old man whose family history revealed possible bipolar affective illness, was used to explore the relationship of dopamine function and manic illness through the use of two drugs with relatively specific effects in stimulating and blocking dopamine receptors, piribedil ET-495 and pimozide. Piribedil as well as d-amphetamine was associated with manic episodes, while pimozide had an antimanic effect. These observations suggest that dopaminergic mechanisms may be involved in the mediation of manic episodes in at least some patients. 32 references. (Journal abstract modified)

002674 Ghose, Karabi; Coppen, Alec; Turner, Paul. Medical Research Council Neuropsychiatry Laboratory, West Park

Hospital, Epsom, Surrey, England **Autonomic actions and interactions of mianserin hydrochloride (Org. GB 94) and amitriptyline in patients with depressive illness.** Psychopharmacology (Berlin). 49(2):201-204, 1976.

The clinical pharmacology of mianserin hydrochloride was studied in patients suffering from a primary depressive illness after steady state plasma concentration of the drug had been achieved. The results were compared with those found with amitriptyline in both open studies and double-blind studies. The two drugs are equally effective in their antidepressive effect. Mianserin hydrochloride appears to be free of anticholinergic effects as assessed by the measurement of salivary volume, pupil diameter, and the interactions with guanethidine and thymoxamine on the pupil. No peripheral adrenergic interaction as studied by the tyramine dose/pressor/response test were observed in patients treated with mianserin hydrochloride (20mg three times daily). 14 references. (Author abstract)

002675 Goodwin, Frederick K.; Rubovits, Randi; Gold, Philip W.; Wehr, Thomas. Section on Psychiatry, Laboratory of Clinical Science, National Institute of Mental Health, 9000 Rockville Pike, Bethesda, MD 20014 **Central monoamine metabolism in depression and mania. (Unpublished paper).** Bethesda, MD, NIMH, 1976. 41 p.

The results of investigations dealing with amine metabolites in the urine and in the cerebrospinal fluid (CSF) of patients with unipolar depression or manic-depressive disease in order to define the underlying biochemical abnormalities in these disorders are presented. The topics discussed are: 1) origins of urinary metabolites; 2) origins of CSF metabolites; 3) amine metabolite findings in affective illness/urinary studies; 4) amine metabolite findings in affective illness/CSF studies; 5) the interpretation of amine metabolite data; 6) clinical sources of variance in amine metabolite studies; 7) critique of existing studies; 8) relationship between metabolite data and the amine hypotheses of affective illness; and 9) amine subgroups as predictors of specific drug response. It is suggested that further attempts to experimentally evaluate single amine theories of affective disorder are not likely to yield unambiguous results and may serve to distract attention from other goals, such as evaluating interrelationships between different amine systems in patients, of identifying subgroups of patients defined clinically, pharmacologically or biochemically, and establishing bridges between these spheres of investigation. 111 references.

002676 Hata, Hiroshi; Yamamoto, Kanichiro; Tozu, Akira; Kase, Tatsuo; Okada, Michio. Department of Psychiatry, Kanto Teishin Hospital, Tokyo, Japan **A double-blind comparison of Doxepin and Nortriptyline on depression.** Japanese Journal of Clinical Psychiatry (Tokyo). 5(2):250-256, 1976.

Results are presented of a double-blind study of the effects of Doxepin and Nortriptyline on depressive and manic-depressive patients. Dosage was varied between 30 and 90mg and symptoms were rated according to the Hamilton Rating Scale. No difference in the beneficial effects of the two drugs was observed, although two patients taking Nortriptyline regressed. For the first week, Doxepin proved slightly better, especially in relieving physical anxiety and hypochondria. The ratios of appearance of side-effects were also the same, even though Nortriptyline treated patients showed more cases of akathisia. It was concluded that the antidepressant effects of Doxepin were sufficient to warrant its use on depressive and manic-depressive patients. 13 references.

002677 Heiser, Jon F.; DeFrancisco, Don. Department of Psychiatry and Human Behavior, California College of Medicine, University of California, Irvine, CA 92668 **The treatment of pathological panic states with propranolol.** American Journal of Psychiatry. 133(12):1389-1394, 1976.

The effects of propranolol, a beta-adrenergic blocking agent, on 10 patients with pathological panic states is reported. Propranolol was effective in treating acute pathological panic, but modest doses of the drug administered for brief periods of time did not alleviate chronic panic attacks associated with agoraphobia. The drug suppressed panic associated with depressive syndromes but did not affect the depression and had no clear effect on anticipatory anxiety. It is suggested that further study of these findings may clarify other clinical problems. 51 references. (Author abstract)

002678 Kabes, J. Vyzkumny Ustav Psychiatricky, Praha 8-Bohnice, Czechoslovakia **/Viloxazin (Vivalan ICI) -- a structurally new antidepressant./** Viloxazin (Vivalan ICI) -- strukturalne nove antidepresivum. Ceskoslovenska Psychiatrie (Praha). 72(4):282-287, 1976.

Viloxazine (Vivalan ICI) is presented as an antidepressant with a novel, bicyclic chemical structure and with a different spectrum of pharmacological properties as compared with the other, known psychotropic drugs. Published clinical experiences with Vivalan in depressed patients obtained in both open and double-blind clinical trials are reviewed. Main advantages of Vivalan ICI are: 1) fast therapeutical effect; 2) minimal occurrence of undesirable side-effects; 3) possibility of use in elderly patients (low cardiotoxicity) and in patients with glaucoma or prostatism; 4) no dietetic restrictions are necessary (interacts well with alcohol); 5) does not cause weight gain even at chronic administration; and 6) possibility of use in epileptics. 31 references.

002679 Kerr, W. C. Spencer Psychiatric Clinic, North-Western General Hospital, Wynyard, Tasmania, 7325 **Lithium salts in the management of a child batterer.** Medical Journal of Australia (Glebe). 2(11):414-415, 1976.

A case history is presented in which a female child batterer's aggressive behavior was successfully managed by treatment with lithium salts. It is suggested that the majority of parents who seriously maltreat their children are people of limited capabilities, are often retarded and are often inadequate socially, and as such, they a really likely to benefit from insight therapy. In lithium treatment, there may be a practical way of helping them. Recent publications have shown that there is increasing interest in the use of lithium salts in the management of psychiatric disorders other than affective disorders, particularly because of its antiaggressive effort. 3 references.

002680 Kielholz, P. University Psychiatric Clinic, Basle, Switzerland **Advances in the drug therapy of affective disorders.** In: Advances in the drug therapy of mental illness. Geneva, World Health Organization, 1976. 168 p. (p. 92-102).

Advances in the use of drug therapy for affective disorders is reviewed. The nosological and phenomenological classification systems are presented. It is noted that the development of antidepressants coincided with a steady increase in the number of patients diagnosed with depressive syndromes and masked depression. Treatment of refractory depressions is also discussed. A review of recent research findings indicates that endogenous depressions are associated with an absolute or relative deficiency of norepinephrine and serotonin at the

synapses and further research to clarify the underlying disorders and to develop a casual oriented form of therapy is advocated. 24 references.

002681 Konig, Liesbeth; Lange, Ehrig; Rossner, Mahnolf; Liefke, Tilo; Uhlig, Birgit; Kursawe, Hubertus K.; Lungwitz, Jurgen. Neurologisch-Psychiatrische Klinik der Medizinischen Akademie Carl Gustav Carus, Fetscherstr. 74, DDR-8019 Dresden, Germany **/Clinical experiences with noxiptiline./** Klinische Erfahrungen mit Noxiptilin. Psychiatrie, Neurologie und Medizinische Psychologie (Leipzig). 28(4):236-242, 1976.

Clinical experiences with noxiptiline in 36 depressives and 1 schizophrenic, 30 to 80 years old, are described. Noxiptiline (Elronon) proved to be a good bipolar thymoleptic agent in the clinical test at three special clinics. Its stimulating effect on the psychomotor function is more pronounced than its sedative action. Therefore, in cases with the anxious, agitated depressive syndrome the additional therapy with a neuroleptic agent or a sedative tranquilizer may be favorable. Noxiptiline is well tolerated even in older patients. The side-effects are the same as those of other known thymoleptics. 8 references. (Journal abstract modified)

002682 Loosen, P. T.; Merkel, U.; Amelung, U. Division of Research, North Carolina Mental Health Department, Station B, Box 7512, Raleigh, 27622 **Combined sleep deprivation and clomipramine in primary depression.** Lancet (London). No. 7977:156-157, 1976.

The combined effects of sleep deprivation and clomipramine are examined in 16 patients with primary depression with: 1) loss of energy, appetite, and libido; 2) sleep disturbances; 3) somatic symptoms of anxiety; and 4) daily rhythms. The following conclusions are reached. Retarded depressions can be treated effectively by a combination of sleep deprivation and clomipramine. The antidepressive action of sleep deprivation can be prolonged by subsequent clomipramine therapy or vice versa. The usual delayed action of clomipramine effect can be hastened by previous sleep deprivation. The application of the findings to tricyclic drugs is not discussed. 20 references.

002683 Mastrosimone, F.; Pepe, G. Universita degli Studi di Napoli, Cattedra di Psichiatria, I Facolta di Medicina e Chirurgia, Naples, Italy **/Clinical contribution on the thymoanaleptic action of the new antidepressant caroxazone (F.I. 6654).**/ Contributo clinico sull'attivita timoanalettica di un nuovo farmaco antidepressivo: Caroxazone-F.I. 6654. Rivista Sperimentale di Freniatria (Reggio Emilia). 100(5):1253-1265, 1976.

A single-blind clinical test of a new antidepressant, caroxazone (F.I. 6654), is reported and evaluated, demonstrating the effectiveness of this new drug. The experimental group consisted of 16 males and 11 females, 21 to 52-years-old, all showing neurotic depression. Caroxazone was administered for periods up to 34 days. Results showed the drug works fast, has no collateral effects, is generally well tolerated, is not addictive, and has complementary anxiolytic action. In contrast to other antidepressants, caroxazone has no hypnotic effect. 29 references.

002684 Messiha, F. S.; Knopp, W. Department of Pharmacology and Therapeutics, Texas Tech. Univ. School of Medicine, P.O. Box 4569, Lubbock, TX 79409 **A study of endogenous dopamine metabolism in Gilles de la Tourette's disease.** Diseases of the Nervous System. 37(8):470-473, 1976.

A longitudinal, blind study of Gilles de la Tourette's disease in a 44-year-old male patient who was nonresponsive to haloperidol therapy indicates that dopamine excretion is related to clinical response. An increased urinary excretion of dopamine and some of its metabolites was associated with the failure of haloperidol therapy. Imipramine, administered to treat the patients' depressive mood that emerged in the course of treatment, decreased the urinary excretion of dopamine and moderately alleviated the symptoms of Tourette's syndrome. The results suggest that monitoring urinary dopamine and 3-methoxytyramine excretion in Tourette's disease may predict the clinical response to pharmacotherapy, and that a dopaminergic mechanism may be associated with this type of motor hyperkinesia. The longitudinal, blind study describes the use of haloperidol, imipramine, and L-dopa in the treatment of a patient suffering from Tourette's disease. The relationship of biogenic amine metabolism to the patients' symptomatology was investigated. 33 references. (Author abstract modified)

002685 no author. no address **Who's got the wrong idea about treating depression? ... a change of attitude to MAOI-tricyclic combinations is obviously needed.** International Drug Therapy Newsletter. 11:29, 1976.

Two recently reported trials in a total of 1000 patients, which confirm the findings of others that a tricyclic and a monoamine oxidase inhibitor (MAOI) combination can be used with no more risk than antidepressants used singly, are noted. Reports since 1966 have attested to the safety of the combination as long as both drugs are started at the same time, only given orally, and the dose of each is lower than when used alone. It is suggested that more reports confirming the safety of the tricyclic-MAOI combination will allow many victims of particular forms of affective illness to receive treatment that they are morally and legally entitled to, but are now denied by all but a few psychiatrists.

002686 no author. no address **How to treat the profoundly depressed patient.** Practical Psychology for Physicians. 3(11):30-33, 37-39, 1976.

In an interview, Heinz Lehmann, a pioneer user of psychopharmacology, discusses the management of the profoundly depressed patient. It is suggested that general practitioners can treat acute depression (patients they reject) more successfully than they can treat neurosis or alcoholism (patients they will treat). The physician must determine whether the depression is pathological or a normal reaction to loss and then he must determine whether it is endogenous or reactive. The danger that the patient might commit suicide is discussed, and it is noted that the depressive mood and suicidal danger in a patient commencing drug therapy will not disappear for 10 days to 2 weeks. It is noted that although lithium is not therapeutic for the majority of depression cases, many physicians think that it is the treatment of choice. Drug treatment including the function of lithium, alternative drugs, increased dosages for patients who do not improve, and the prospects for new drugs are discussed. The use of psychosurgery for those patients who resist all treatments, family participation in treatment, and how to talk to depressed people are discussed.

002687 Ohi, Masaki; Kasahara, Yoshi. Department of Psychiatry, Nagoya University, Nagoya, Japan **Prepubescent depression (4th report) -- experiences with the efficacy of lithium carbonate.** Psychiatria et Neurologia Japonica (Tokyo). 78(12):831, 1976.

At the 92nd Eastern Japan General Psychoneurological Symposium held in July 1975, at Nagoya, Japan, a report was made on the use of lithium carbonate on five patients under

the age of 15 who were suffering from depression. Lithium was tried because of the special characteristics of depression in children: short lived and recurrent, and generally not respondent to tricyclic or major tranquilizers. Three of the patients had classic manic-depression and two had unspecified depression. The average age was 12.2; administration of the drug from 3 to 5.5months in doses of from 600 to 100mg. In preventing recurrence, it was effective in four cases and slightly effective in one. The only side-effect noted was nausea and diarrhea in one case.

002688 Owen, Frank; Bourne, Rachel; Crow, Timothy J.; Johnstone, Eve C.; Bailey, Alan R.; Hershon, Howard I. Division of Psychiatry, Clinical Research Centre, Watford Road, Harrow, Middlesex HA1 3UJ, England **Platelet monoamine oxidase in schizophrenia: an investigation in drug-free hospitalized patients.** Archives of General Psychiatry. 33(11):1370-1373, 1976.

Platelet monoamine oxidase (MAO) activity was investigated in 60 male chronic schizophrenics, mean age 57 and mean length of illness 26 years, and in 70 normal male controls, mean age 47, selected from among routine insurance medical examinees who had no family history of mental illness. Of the 60 patients, 54 had never received antipsychotic medication and the remaining 6 had not received medication for at least 6 months. The MAO activity in the patients group did not differ from that of the controls for either tyramine or tryptamine. There was no difference in platelet MAO activity between patients with or without positive symptoms (hallucinations, delusions, and formal thought disorder). Platelet MAO activity did not correlate with scores on the Krawiecka Modified Inpatient Rating Scale, nor did it correlate with age or serum iron level. There were no differences in platelet MAO activity in nine schizophrenics receiving depot flupentixol decanoate or fluphenazine decanoate for 6 months and in a similar group of patients not taking such medication. Patients receiving medication showed an increase in MAO activity after 6 months. 26 references.

002689 Planche, R.; Gathier, M.-C.; Lambert, J. no address **/Description of a simple graphic model enabling comparison of the development of depressive states./** Description d'un modele graphique simple permettant de comparer l'evolution des etats depressifs. Annales Medico-Psychologiques (Paris). 2(4):678-686, 1976.

A graphic model describing different elements of depressive states was described at the October 1976 session of the Societe Medico-Psychologique. The Hamilton scale was used to determine the effectiveness of the new antidepressant Doxepine as compared to two thymoanaleptics. One of the researchers was informed, while the other carried out a single-blind study. Results indicate statistical correlations (both researcher/physicians reported the same improvements) after 8, and 21 days respectively in both endogenic and neurotic depressions. The advantages of the graphic model in objectively evaluating depression are discussed.

002690 Poeldinger, W. J. Psychiatrisch-Neurologische Klinik, University of Vienna, Vienna, Austria **Drug therapy in depressive states: factors in suicide prevention.** In: Essman, W., Current developments in psychopharmacology. New York, Spectrum, 1976. 393 p. v. 3. (p. 179-196).

The use of psychotropic drugs, especially antidepressants, for suicide prevention in depressed patients is discussed. The diagnosis of depression and classification of the type of depression present based on etiology and on qualitative and quantitative evaluation of individual symptoms are reviewed. A weighting scale of factors for assessing the risk of suicide in an individual patient is presented. Intense suppression of suicidal tendencies may be accomplished by administration of neuroleptics with a potent sedative component action or by nonneuroleptic tranquilizers having a sedative effect. Suppression of less intense suicidal tendencies may be accomplished by administration of antidepressants with sedative effects, while modification of the underlying depression may be achieved by administration of antidepressants with a mood elevating effect. Central stimulants may activate suicidal tendencies, and antidepressants with an activating component should be used in suicidal patients only in combination with a drug having a sedative effect, if at all. It is pointed out that psychopharmacotherapy is an adjunct, not an alternative, to psychotherapy. It is stated that psychotropic drugs can be used effectively only if they are applied within the framework of a comprehensive plan of psychotherapy including a stable patient/doctor relationship. 26 references.

002691 Rackensperger, W.; Fritsch, W.; Schwarz, D.; Stutte, K. H.; von Zerssen, D. Max-Planck-Institut fur Psychiatrie, Kraepelinstrasse 10, D-8000 Munich 40, Germany **/Effect of the beta-receptor blocker propranolol on mania./** Wirkung des Beta-Rezeptoren-Blockers Propranolol auf Manien. Archiv fur Psychiatrie und Nervenkrankheiten (Berlin). 222(2/3):223-243, 1976.

The effect of propranolol, a beta-adrenergic blocker, was studied in six patients with mania. The one male and five females ranged in age from 25 to 47 years. Case reports are given of the six patients. The maximal daily dosage ranged from 200 to 2320mg, and treatment ranged from 4 to 15 days. Patients were rated on the Inpatient Multidimensional Psychiatric Scale. Good or very good improvement occurred in four patients, but all four patients relapsed when the drug was withdrawn. Side effects were hypotension, bradycardia, hypertension, precordial pain, abdominal pain, insomnia, and gastric bleeding. 44 references.

002692 Renfordt, Ernst; Busch, Helmut. Psychiatrische Klinik, Freie Universitat, Berlin, Germany **Time-blind analysis of TV-stored interviews: an objective method to study antidepressive drug-effects.** International Pharmacopsychiatry (Basel). 11(3):129-134, 1976.

A new method of evaluating the time course of antidepressive drug effect, based on time blind analysis of TV stored tapes of interviews recorded during drug trials, is described. Twenty depressive inpatients received either amitriptyline or mianserin for 20 days in a double-blind trial. TV tapes of interviews with the subjects during the drug trial were presented in a randomized sequence to raters who ranked each patient's tapes in terms of the degree of depression shown during the interview. It is posited that this method of evaluation has the advantage of the rater being "blind" to the duration of the treatment. Results show that patients treated with amitriptyline showed a continuous amelioration of depression throughout the drug trial, while those subjects treated with mianserin showed an amelioration of depression that was not constant in time. 10 references. (Author abstract modified)

002693 Riley, Graham J.; Shaw, David M. Biochemical Psychiatry Lab., Dept. of Psychological Medicine, Welsh National School of Medicine, Cardiff CF4 7XB, Wales **Total and non-bound tryptophan in unipolar illness.** Lancet (London). No. 7997:1249, 1976.

Methodological differences are used to explain the contradictory research on patients with unipolar affective disorders having low levels of nonbound tryptophan in their plasma. Controls were tested against patients who had fasted overnight, had no antidepressants for a week, and no phenothiazines for at least a month. Results of the experiment indicated that tryptophan/albumin binding is normal at physiological temperatures and pH in depressive illness, and is not affected by tricyclic drugs. It is suggested that changes in cellular pools of tryptophan in patients during or after unipolar illness might be due to alteration in cellular binding of tryptophan to albumin. Patients not responding to tricyclics had a lower concentration of tryptophan in their plasma than those who recovered. 13 references.

002694 Roccatagliata, G.; Cocito, L.; Albano, C.; Gandolfo, C.; Abbruzzese, G.; Primavera, A. Clinica delle malattie nervose e mentali dell'Universita di Genova, Genova, Italy **/Preliminary study of the treatment of endogenous depression with bromoergocryptine./** Trattamento delle depressioni endogene con bromo-ergocriptina studio preliminare. Rassegna di Studi Psichiatrici (Siena). 65(3):541-547, 1976.

Bromoergocryptine was administered to three endogenous depressive females and seven males, 33 to 65 years old. Therapeutic results were evaluated with the Hamilton Rating Scale for Depression (HRSD). Results showed two patients were restored to full health, four showed noticeable improvements, two showed slight improvement, and two showed no improvement at all. Two attached tables contain the full results of the HRSD. Conclusion was that bromoergocryptine seems to be mainly effective on symptoms such as asthenia and psychomotor inhibition. 14 references.

002695 Rybakowski, J.; Szajnerman, Z. Department of Psychiatry, Academy of Medicine, Ul. Szpitalna 27/33, 60-572 Poznan, Poland **Lithium-magnesium relationship in red blood cells during lithium prophylaxis.** Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 9(5):242-246, 1976.

The relationship between lithium and magnesium metabolism in red blood cells was studied in 30 patients receiving propylactic doses of lithium carbonate at the outpatient clinic. The 13 males and 17 females ranged in age from 18 to 68 years old. There were 23 patients with manic-depressive psychosis and seven patients with unipolar depression. The dose of lithium was constant for each patient and ranged from 500-1500mg/day, and the patients had been on lithium for 3 months to 4 years, with a mean of 2.2years. Blood was drawn from the patients in the morning before the first lithium dose, and serum Li, Mg, and hematocrit were measured. Measurements were done twice in each patient with a 6 to 8 week period intervening. The ratio of serum lithium to red blood cells was higher in women than in men, particularly in bipolar patients. The magnesium concentration in erythrocytes correlated negatively with the serum lithium level and with the lithium concentration in red blood cells. Serum magnesium levels did not correlate with lithium concentration. The results suggest that the magnesium concentration in red blood cells may play a role in the lithium penetration of red blood cells. 15 references.

002696 Rybakowski, Janusz; Chlopocka-Wozniak, Maria. Klinika Psychiatryczna AM, 27/33 ul. Szpitalna, 60-572 Poznan, Poland **/A study of interdependence between erythrocyte lithium index and the clinical state of patients with affective disorders treated prophylactically with lithium salts./** Badania zaleznosci wskaznika krwinkowego litu od stanu klinicznego chorych z zaburzeniami afektywnymi leczonych profilaktycznie litem. Psychiatria Polska (Warszawa). 10(5):509-514, 1976.

Interdependence between the erythrocyte lithium index and the clinical state of patients with affective disorders treated prophylactically with lithium salts was studied in 34 patients during a 12 to 24 month period. Symptoms of manic or depressive syndrome appeared in 14 patients during this period, and in 7 of the 11 patients who developed manic episode the average value of the index was significantly higher than the average value during remission. Further pathogenic and clinical studies are indicated. 10 references. (Journal abstract modified)

002697 Saldana Hernandez, Oscar Humberto. Fray Bernardino Alvarez, Consulta Externa del Hospital Psiquiatrico, Mexico City, Mexico **/Amitriptyline in the treatment of depression./** La amitriptilina en al tratamiento de la depresion. Neurologia - Neurocirugia - Psiquiatria (Mexico City). 17(3):153-158, 1976.

Oral amitriptyline was evaluated clinically in the treatment of 14 male and 16 female outpatients, aged 17 to 59 years, selected at random, and who presented depression (16 neurotic, 3 reactive, 11 involutional). Four had had no prior antidepressive treatment, and the rest had had medication with poor results. The study ran for 12 weeks, with 15 patients showing improvement by the fourth week, 8 by the fifth week, 1 by the sixth; 5 showed no change. Dosage was begun with tablets of 50mg three times daily in three patients, but this dosage was considered excessive and was slowly reduced to a minimum of 25mg per day by the end of the study. Side-effects disappeared by adjusting the dosage. Seventeen patients showed total improvement, 8 moderate improvement and 5 showed no change. 4 references. (Journal abstract modified)

002698 Schou, Mogens. no address **Advances in lithium therapy.** Current Psychiatric Therapies. 16:139-153, 1976.

Lithium carbonate and its use in therapy of manic-depressive disorders is discussed. Lithium's biochemical mode of action is outlined. Proven and suggested uses of lithium maintenance treatment are described; established psychiatric indications for lithium treatment are mania and recurrent manic-depressive disorder. Pharmacokinetics and the mechanism of poisoning are described; initiation, monitoring through serum lithium concentration, and maintenance of lithium therapy by the physician are outlined. Lithium treatment during pregnancy and delivery, treatment failure, side effects, and lithium poisoning are discussed. 11 references.

002699 Smulewicz, A. B. no address **/Use of sidnocarb in treating patients in asthenic or depressive states./** Stosowanie Sidnokarbu w leczeniu stanow astenicznych i depresyjnych. Psychofarmakoterapia Schizofrenii Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 229-232).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, the use of sidnocarb in treating patients in an asthenic state or those suffering depression is reported. The drugs signocarb and azafen, which were synthesized in the USSR, are effective psychotropic agents whose results can be observed within 1/2 hour to 1 hour. The drugs were tested on 116 patients with various psychiatric disorders, including schizophrenia. The most effective results were obtained for patients suffering from asthenic depression or other adynamic depressive states.

002700 Takahashi, Saburo; Takahashi, Ryo; Masumura, Isao; Miike, Akira. Department of Psychiatry and Neurology, Kyoto Prefectural University of Medicine, Kyoto, Japan **Measurement of 5-hydroxyindole compounds during L-5-HTP treatment in depressed patients.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 30(4):463-473, 1976.

Urinary excretion levels and plasma concentrations of three 5-hydroxyindole compounds were measured during treatment of hospitalized depressed patients with an immediate serotonin precursor, L-5-hydroxytryptophan (L-5-HTP). Approximately 70% of the orally administered dose of L-5-HTP was recovered from the urine of depressed patients. Major part of urinary indoleamine metabolites was free and conjugate 5-HIAA. Excretion levels of these compounds in urine were not consistently altered in the depressed patients as compared to those in normal subjects. Clinical response to L-5-HTP treatment appeared to have some correlation with the biochemical measures in the depressed patients, that is, nonresponders exhibited significantly lower excretion levels of 5-HT and 5-HIAA in urine, and lower plasma levels of 5-HT than responders. Administered L-5-HTP may not be fully utilized to the depressed patients who did not react to the agent. 39 references.

002701 Taranskaya, A. D. Khar'kovskiy nauchno-issledovatel'skiy institut nevrologii i psikhiatrii, Kharkov, USSR **/Dynamics of clinico-pathophysiological traits of senile psychosis under the influence of azafen./** Dinamika kliniko-patofiziologicheskikh osobennostey psikhozov v pozdnem vozraste pod vliyaniem azafena. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova (Moskva). 76(3):440-443, 1976.

A clinicopathological study of single doses and subsequent maintenance therapy with azafen on the higher nervous activity of presenile mental patients (67 cases) revealed that its action depends on the dosage of the preparation and the nosological syndrome. Depressive involutionary psychoses can be controlled by azafen in doses of up to 75mg daily. Doses of 25mg/day reduce or completely eliminate the altered consciousness syndrome caused by cerebrovascular disorder. Depressive syndrome in manic-depressive psychosis in the aged can be arrested by 150 to 200mg/day. 2 references. (Author abstract modified)

002702 van Kammen, Daniel P.; Murphy, Dennis L. NIMH, Bldg. 10, Room 4N214, Bethesda, MD 20014 **Antidepressant response prediction by amphetamine. (Unpublished paper).** Bethesda, MD, NIMH, 1976. 1 p.

The antidepressant responses to imipramine and to lithium carbonate of 20 unipolar depressed patients were compared to their responses to amphetamine, in a study of the predictive power of responses to amphetamine therapy. A self-rated mood and behavior checklist which correlates highly with observer rated behavior in depressed patients was used. Several different response patterns to amphetamine were observed, with euphoria, reduced depression, activation or dysphoria responses predominating in different patients. The comparisons between the amphetamine responses and subsequent therapeutic antidepressant responses were clearest for lithium carbonate treatment.

002703 Van Putten, Theodore. no address **Lithium in previous treatment failures.** Current Psychiatric Therapies. 16:155-162, 1976.

Because there is indication that lithium may be useful in nonmanic-depressive conditions, a trial of lithium carbonate was given to 39 hospitalized patients with previously intractable mental illness. These patients had not responded to intensive interactional and rehabilitative approaches over a period of years. Of the 39 previous treatment failures started on lithium, 15 patients improved; 9 improved dramatically. The unexpected improvers were categorized as: 1) patients with nonremitting manic-depressive illness; 2) patients with psychotic excitements; or, 3) patients with character disorders. Other improved conditions included mixed manic-depressive illness, intractable psychotic depression, and chronic unipolar mania. It is suggested that a lithium sensitive psychosis in a close relative should raise the consideration of a lithium trial. Contraindications are seen as including circulatory disease, kidney disease, general debilitation, advanced age, and pregnancy. It is concluded that the best candidates for a lithium trial are patients in whom mood states such as irritability, anger, excitement, and impulsive aggressivity are core problems. 29 references.

002704 Venalainen, Eino; Puhakka, Pertti. Harjamaki Hospital, SF-7870 Harjamaki, Finland **Chlorimipramine and amitriptyline in the treatment of depression.** Psychiatria Fennica (Helsinki). No. 7:173-176, 1976.

A study of chlorimipramine and amitriptyline in the treatment of depression, based on analysis of the clinical effects compared in a double-blind trial with depressive patients, is presented. The sample included 35 hospitalized patients, 18 to 60-years-old, (27 males and 8 females), who had not previously been treated with antidepressants. Results indicated that both chlorimipramine and amitriptyline proved to be effective and suitable for treatment of various kinds of depression. Side-effects were observed in only seven patients, and in only one case was drug treatment discontinued. It is indicated that chlorimipramine treatment should continue for at least 2 weeks because beneficial results may only be evidenced at a later stage. 16 references.

002705 Wirz-Justice, Anna; Puhringer, Wolfgang; Hole, Gunter. Psychiatrische Universitatsklinik, CH-4025 Basel, Switzerland **Sleep deprivation and clomipramine in endogenous depression.** Lancet (London). No. 7991:912, 1976.

In a letter to the editor of Lancet, the use of sleep deprivation and clomipramine in endogenous depression was examined. Clomipramine and maprotiline appear to be useful for investigating a sleep deprivation therapeutic model. Although there are patients whose improvement after sleep deprivation appears to last, the acute and transient effects of sleep deprivation is recommended as a provocation method. It is concluded that the sleep deprivation method is a useful model for biochemical studies of short-term affective changes, and it may also be a simple clinical screen for a more rational and effective antidepressant therapy. 8 references.

002706 Wolff, Anthony. no address **Medicine for melancholy.** Saturday Review. February 21:34-35, 1976.

Depression and its pharmacotherapeutic treatment are briefly discussed. Despite the prevalence of depression surprisingly little is known about its etiology. The traditional treatment for depression, psychoanalysis, often failed to justify the heavy costs and time required. Three families of drugs are now providing relief for the depressed: monoamine oxidase (MAO) inhibitors; tricyclic antidepressants, and lithium, which is particularly effective in the treatment of manic disorders. Once the proper combination or dosage of drugs has been established and reached a therapeutic level in the brain, the patient subject to recurrent attacks can be placed on a low

maintenance dosage. Research falls behind clinical use however and the identification of patients and disorders responsive to such therapy and the biochemical mechanisms involved have not yet been fully elucidated. Lithium in the treatment of affective disorders has been particularly subject to both professional and popular controversy.

002707 Yoshida, Noboru; Nakano, Keijiro; Koike, Kenji; Goto, Yoshio; Haga, Yukihiko; Ohi, Masaki; Nakane, Kiyoshi. Toyogawa Citizen's Hospital, Toyogawa, Japan **Experiences in using lithium carbonate -- especially with mania and manic depressive cases.** Psychiatria et Neurologia Japonica (Tokyo). 78(12):830-831, 1976.

At the 92nd Eastern Japan General Psychoneurological Symposium held in July 1975, at Nagoya, Japan, statistics were presented on the efficacy and the side-effects of lithium carbonate use to prevent mania and manic-depression in eight Japanese hospitals (60 total patients). It was found very effective in 25.5% of the cases, effective in 41.2%, and slightly effective in 19.6% of the cases. Side-effects noted were loss of appetite, thirst, nausea, and diarrhea, and were discovered in 24 of the 60 patients. No more serious side-effects, were noted. To counteract side-effects dosage was reduced and phenylthiazine drugs were also administered. This retained therapeutic effects while lessening side-effects.

002708 Ziegler, Vincent E.; Clayton, Paula J.; Taylor, John R.; Co, Bun Tee; Biggs, John T. Dept. of Psychiatry, Washington University School of Medicine, 4940 Audubon Ave., St. Louis, MO 63110 **Nortriptyline plasma levels and therapeutic response.** Clinical Pharmacology and Therapeutics. 20(4):458-463, 1976.

Depressed outpatients (N=18) were treated for 6 weeks with a mean daily dose of 121mg of nortriptyline to investigate the relationship between plasma levels and therapeutic responses. Therapeutic response was monitored by the Zung Self-Rating Depression Scale and the Hamilton Depression Scale administered by two psychiatrists blind to the tricyclic used, dose, and plasma levels. Eight patients recovered by the fourth week and 12 by the sixth week. There was a positive correlation between the weekly Hamilton scores and the weekly nortriptyline levels. The 9 patients with mean plasma levels between 50 and 139ng/ml had a better therapeutic response after 6 wk measured by percent recovered, Zung score, and Hamilton score than the 9 patients with mean plasma levels between 140 and 260ng/ml. 16 references. (Author abstract modified)

10 DRUG TRIALS IN NEUROSES

002709 Auron Zaltzman, David. Facultad de Psicologia, Universidad Nacional Autonoma de Mexico, Mexico City, Mexico /**Amitriptyline hydrochloride in the treatment of anxiety and insomnia, and as a tranquilizer.**/ El clorhidrato de amitriptilina en el tratamiento de la ansiedad y el insomnio, y como tranquilizante. Neurologia - Neurocirugia - Psiquiatria (Mexico City). 17(3):165-169, 1976.

An open, noncomparative study with weekly clinical evaluations was made of 30 outpatients of both sexes aged 16 to 70 years in order to test the tranquilizing effectiveness of amitriptyline hydrochloride in the treatment of anxiety insomnia, and depression. Twenty-three patients completed 12 weeks of treatment and seven stopped treatment before completion for differing reasons. Dosages varied from 25 to 100mg daily, with a median dose of 50mg. Twenty-three patients showed mild side effects that disappeared without specific treatment. Improvement began the first or second week; by the end of 12 weeks, 17 patients were considered cured, 16 improved, and 7 showed no change. 4 references. (Journal abstract modified)

002710 Broszkiewicz, Ewa; Gatarski, Julian; Polewka, Andrzej; Zelewska, Maria. Klinika Psychiatryczna AM, Kopernika 21, 31-501 Krakow, Poland /**Indications for lithium carbonate prophylaxis.**/ Problem wskazan do profilaktycznego stosowania litu. Psychiatria Polska (Warszawa). 10(6):647-653, 1976.

Indications for lithium carbonate prophylaxis are presented, based on histories of patients under psychiatric treatment. Patients with severe long-term cyclotyhmia were the most eager and persistent in continuing this treatment, and best results were obtained in these cases. In patients with a brief history of illness, insufficient motivation for treatment was observed. Results indicate that patients with mixed psychosis did not respond as well to prophylaxis as patients with pure cyclothymia. 29 references. (Journal abstract modified)

002711 Bueno, Marco Aurelio. Apartado Aereo 6824, Cali, Valle, Columbia /**Protriptyline: the relationship between plasma concentrations and the clinical effect on depressed male patients.**/ Protriptilina: relacion entre las concentraciones plasmaticas y el efecto clinico en pacientes hombres deprimidos. Revista Colombiana de Psiquiatria (Bogota). 5(4):431-438, 1976.

To study the effectiveness of orally administered protriptyline 36 hospitalized males, diagnosed as neurotic depressives, and whose score on the Zung depression scale was greater than 75% on admission, were selected for treatment. The average age of the subjects was 37 years, all were in satisfactory physical condition, and none received drug therapy until the second week in hospital. Diazepam was used when needed as a sedative. Five different dosage schedules were given according to body weight, administered in four equal daily doses. The study was double-blind, 6 of the 36 subjects receiving placebos. Blood samples were taken twice weekly and analyzed for drug concentration. Several undesirable side-effects were found in the patients receiving 0.8and 1.0mg per kg per day. The oral dosage and plasma concentration were found to be closely related, and a stable equilibrium was reached after 3 to 4 weeks. Clinical improvement was most evident with oral daily dosages between 0.4and 0.8mg per kg. The importance of individual evaluation by the psychiatrist is emphasized, in order to avoid the discontinuance of the drug before reaching the appropriate therapeutic action time and dosage level.

002712 Byrne, D. G. Social Psychiatry Research Unit, Australian National University, Canberra, Australia **Vigilance and arousal in depressive states.** British Journal of Social and Clinical Psychology (London). 15(Part 3):267-274, 1976.

An experiment was conducted to investigate predictions of vigilance performance among depressive patients, based on the assumption that vigilance would vary in a predictable manner with level of arousal, and that levels of arousal among diagnostic categories of depressive patients are well known. It was found that psychotic depressives, presumed to be hypoaroused relative to normals, exhibited poor signal detection performances and committed few false positive errors relative to normals. This was consistent with predictions. Neurotic depressives, presumed to be hyperaroused relative to normals, detected fewer signals than did normals, but also made more false positive errors than normals. Again this was consistent with predictions. A measure of arousal in experimental subjects, namely barbiturate tolerance, was found to relate

directly to the false positive error rate in all subjects. The relationship between arousal and total signal detection rate was significantly curvilinear, and an inverted "U" (quadratic) function provided the best fit. It was concluded that vigilance performance is a function of at least that component of arousal measured by barbiturate tolerance. 14 references. (Journal abstract modified)

002713 Cardenas Trigos, Mario. Escuela Nacional de Estudios Profesionales, Plantel Iztacala, Universidad Nacional Autonoma de Mexico, Mexico City, Mexico **/Clinical evaluation of amitriptyline hydrochloride in the treatment of depression./** Valoracion clinica del clorhidrato de amitriptilina en el tratamiento de la depresion./ Neurologia - Neurocirugia - Psiquiatria (Mexico City). 17(3):139-144, 1976.

To determine the usefulness of amitriptyline hydrochloride in the different forms of human depression, the drug was administered to 30 patients ages 18 to 66 years, presenting depressive states, principally reactive depression. Fifteen subjects were chosen from a private practice and the other fifteen were employees of a public institution. Dosage was 75mg per day, taken in three doses, and treatment lasted 3 months. Observations were performed once weekly. The drug was very effective in 13 subjects and moderately effective in 15. Tolerance was good, and in only one case was the treatment terminated because of side-effects. Daytime sleepiness, tachycardia and weight gain were the most frequently observed side-effects. 3 references.

002714 de Renteria, Carmen D. Servicio de Higiene Mental, Direccion General de Asistencia Social, Secretaria de Salubridad y Asistencia, Mexico City, Mexico **/Clinical evaluation of amitriptyline in the treatment of psychogenic disturbances./** Valoracion clinica de la amitriptilina en el tratamiento de los trastornos psicogenos. Neurologia - Neurocirugia - Psiquiatria (Mexico City). 17(3):159-163, 1976.

Clinical evaluation of amitriptyline in the treatment of psychogenic disorders was carried out, using from one to four .25mg doses per day orally. Nineteen of the patients were male and 11 female, ages of 18 and 55, and all presented affective disturbances: depression (16), inadequate affect (6), anxiety (8). Treatment lasted 12 weeks, and clinical improvement was observed from the second to the fifth week, with mild side-effects that did not require treatment. Psychotherapy was instituted during treatment. Final results were: 23 good improvement, 4 some improvement, and 3 no change. 4 references. (Journal abstract modified)

002715 Delwardre, G.; Delwardre, C. "Val-des-Bois," F-13009, Marseille, France **/Test of a new anxiolytic, lorazepam, with the use of the electroaffectrogram (EAG)./** Etude d'un novel anxiolytique, le Lorazepam, a l'aide de L'electroaffectogramme (E.A.G.). Psychologie Medicale (Paris). 8(8):1289-1308, 1976.

A paper presented at the 4th Meeting of Methodology of Research in Psychiatry, Marseille, April 1975, reports a clinical trial of a new anxiolytic, lorazepam, utilizing the electroaffectogram, or a measure of galvanic skin response, for objective determination of anxiety dynamics. The action of lorazepam was recorded in anxiety neurosis, phobic neurosis, alcoholism and insomnia; lorazepam in combination with a thymoanaleptic was tested in depressive state, hypochondriac neurosis, endogenous depression and schizophrenia; the electroaffectogram also was recorded with placebo. It is concluded the study enabled objective determination of the therapeutic efficacy of lorazepam in several psychiatric nosologies. 15 references.

002716 Diaz Solano, Carlos. no address **/Amitriptyline in the treatment of anxiety and insomnia, and as a tranquilizer./** La amitriptilina en al tratamiento de la ansiedad y el insomnio, y como tranquilizante. Neurologia - Neurocirugia - Psiquiatria (Mexico City). 17(3):133-138, 1976.

To establish the efficacy of amitriptyline as a tranquilizer, 30 outpatients, 22 females and 8 males, selected at random because of the diagnoses of insomnia, anxiety, psychomotor disturbances, loss of drive, and anxiety with somatic manifestations, and administered 25 mg amitriptyline, one to four times a day for 12 weeks. Results were satisfactory in 25 of the subjects, with improvement observed from the second week of therapy. Side-effects were minimal. It is concluded that amitriptyline is of great effectiveness in the treatment of anxiety neuroses most commonly observed in clinical practice. 5 references. (Journal abstract modified)

002717 Gabrielli, Filippo. Istituto di Psichiatria dell'Universita di Genova, Genoa, Italy /**Water poisoning and diabetes insipidus: a propos compulsive water drinking and dysthymia./** Tossicomania da acqua e diabete insipido. A proposito di assunzione coattiva d'acqua in episodio distimico. Archivio di Psicologia, Neurologia e Psichiatria (Milano). 37(4):525-543, 1976.

An overview of compulsive water drinking is given, suggesting that inbibing abnormal amounts of water is potentially dangerous to the patient because of water intoxication, diabetes insipidus or psychogenic polydypsia. In view of prior research in water intoxication it is suggested that a person can become addicted to and dependent upon water just as he can upon alcohol or drugs. In a clinical case presented a 38-year-old female was consuming four liters of water a day and reported drowsyness, retardation, fatigue and vision impairment, and showed signs of depression and mood disturbances. Diabetes insipidus was immediately excluded on the basis of clinical tests. Psychotropic therapy was begun with amitriptiline and oxazepan for a 1 month period and results were so good that the subject did not have to be hospitalized. It is concluded that water intoxication can suggest acute psychotic disorders, personality problems, physical problems such as diabetes, and temporary psychological imbalance. Both psychotherapy and psychopharmacologic drugs can give acceptable results in curbing compulsive water consumption. 34 references.

002718 Gomez Lozano, Pedro. Departamento de Psiquiatria, Universidad Javeriana, Bogota, Columbia **/Intravenous lorazepam in acute anxiety crises./** Lorazepan intravenoso en las crisis de ansiedad aguda: un reporte preliminar en 60 casos. Revista Columbiana de Psiquiatria (Bogota). 5(4):394-401, 1976.

To evaluate the effectiveness of lorazepam in the control of anxiety, insomnia, and agitation in patients with severe psychoneurotic profiles, 40 patients, (31 women, 9 men, ages 14 to 70 years) were given 3mg intravenous doses of lorazepam during critical episodes of acute anxiety (33 cases) or hysteria (7 cases). If the patients did not improve after the initial dose, a second dose was administered after 1 hour, and up to 4 in 24 hours. The symptoms completely disappeared in 95% of the cases after 5 to 10 minutes, and only 3 required more than 1 injection to effect the improvement. The greatest effect noted was sedation and relaxation. Twenty four patients fell asleep after the injection, and only two remained tense. No unfavorable side-effects were noted. The results are compared with those of a double-blind experiment by Bacellar (1975). 8 references.

002719 Husmann, F. Kurklinik, D-6277 Camberg/Taunus, Germany /**Mazindol (Teronac) in the treatment of predominantly alimentary obesity.**/ Mazindol (Teronac zur Behandlung der vorwiegend alimentar bedingten Adipositas. Medizinische Welt (Stuttgart). 27(40):1904-1908, 1976.

The anorexic efficacy of Mazindol (5-p-chlorophenyl-2,5-dihydro-3H-imidazo(2,1-a)isoindol-5-01) was tested in 40 patients with predominantly alimentary obesity. Patients received 3mg Mazindol daily in 1mg doses 1 hour before meals. A reducing diet of 800 to 1200 calories was recommended during therapy, lasting 4 to 6 weeks. Laboratory specimens were obtained at weekly intervals. Average weight loss after 6 weeks was 11.4kg. Blood pressure, respiration, and pulse rates were significantly lower. Most cases with previously abnormal blood sugar, cholesterol, and triglyceride values achieved normal levels after treatment. Side-effects included dryness of the mouth, insomnia, headache, nervousness, vertigo, and fatigue. One patient terminated treatment because of psychogenic vomiting. Mazindol is considered to be an effective, well tolerated anorexic. 11 references.

002720 Johnson, Gordon; Singh, Bruce; Leeman, Marsha. Department of Psychiatry, University of Sydney, Sydney, New South Wales 2006, Australia **Controlled evaluation of the beta adrenoceptor blocking drug oxprenolol in anxiety.** Medical Journal of Australia (Glebe). 1(24):909-912, 1976.

The effectiveness of the beta-adrenoceptor blocking drug oxprenolol in the treatment of primary clinical anxiety was studied in 38 patients. A controlled double-blind evaluation of oxprenolol versus diazepam and placebo was carried out. The results of the trial showed diazepam to be generally more effective and to produce a more rapid effect of symptom reduction than oxprenolol. The role of beta-adrenergic blocking drugs in the treatment of clinical anxiety and related syndromes is discussed. 17 references. (Author abstract)

002721 Kurland, Morton L. Desert Hospital Mental Health Center, P.O. Box 1627, Palm Springs, CA 92262 **Neurotic depression: an empirical guide to two specific drug treatments.** Diseases of the Nervous System. 37(8):424-431, 1976.

Two specific drug treatments, using a group of neurotically depressed patients with anxiety, are described. In these patients, treated with a phenothiazine (thioridazine) or a benzodiazepine (diazepam), the average severity of crucial symptoms such as depressed mood and ideas of suicide decreased by over 50% and did so during the initial 4 weeks of treatment, comprising the span of this double-blind study. The severity of many other related symptoms decreased by almost 1/2 during that period. The results revealed a moderate but fairly consistent advantage for thioridazine for most symptoms. Details of differential effectiveness, as well as features and problems in the treatment of neurotic depression by the practitioner are described. 9 references. (Author abstract modified)

002722 Lader, Malcolm. Institute of Psychiatry, De Crespigny Park, London, England **Somatic and psychic symptoms in anxiety.** In: Carlsson, C., Neuro-psychiatric effects of adrenergic beta-receptor. Munich, Urban & Schwarzenburg, 1976. 120 p. (p. 21-28).

In a paper presented at a symposium on neuropsychiatric effects of adrenergic beta-receptor blocking agents held in Copenhagen, October 1975, it was reported that patients exhibiting various manifestations of anxiety were treated with placebo, diazepam, and beta-adrenoceptor blocking agents (BABA). It was found that patients complaining primarily of somatic symptoms showed some response to BABA, whereas those with predominantly psychic symptoms failed to respond to BABA drugs but did respond to diazepam. This indicates that a symptom profile should be drawn up for each patient. If drug treatment is deemed appropriate, a combination of centrally acting benzodiazepine and a peripherally acting beta-blocker should be used. The treatment for patients with predominatly psychic symptoms should emphasize the benzodiazepine, whereas that for patients with somatic symptoms should concentrate on the beta-blocker. 28 references.

002723 Meiu, Gh.; Zahariade, St.; Patrascu, F.; Arion, J. Spitalul clinic Dr. Gh. Marinescu, Bucuresti, Romania /**Aspects of psychosocial recovery under relaxant therapy -- autogenic training -- in marginal psychiatry.**/ Unele aspecte de recuperare psihosociala in conditiile aplicarii terapiei relaxante -- training autogen -- in psihiatria marginala. Neurologie, Psihiatrie, Neurochirurgie (Bucuresti). 21(4):291-294, 1976.

Use of psychopharmacotherapy and classical psychotherapy in combination with the relaxation therapy method of Schultz in a group of 100 patients with neuroses and psychopathies is described. Results were evaluated 3 years after hospitalization by clinical and psychological reexamination and results were compared with a control group of similar structure. It is concluded the autogenic training potentiated the drug treatment and psychotherapy and reinforced and established their therapeutic effects. (Journal abstract modified)

002724 Misurec, J.; Slama, B.; Nahunek, K. Organizacne metodicke oddeleni KUNZ, Brno, Czechoslovakia /**Pyrithioxin (encephabol) in the treatment of patients with organic psychosyndrome in involution: clinical, EEG and experimental psychological study.**/ Pyrithioxin /encephabol/ v lecbe nemocnych s organickym psychosyndromem involuci Klinicka, elektroencefalograficka a experimentalne psychologicka studie. Ceskoslovenska Psychiatrie (Praha). 72(1):14-23, 1976.

Pyrithioxin and placebo were given for 6 weeks each in a double-blind crossover design to patients with organic psychosyndrome in involution. Clinical changes were evaluated with a 38 item rating scale and the following psychological tests were repeatedly done: reaction time, flicker fusion test, tapping, numeric square, paired-associations, and the Benton test. An electroencephalogram (EEG) was registered in an acute test 4 hours after a single dose of 300mg of pyrithioxin, then after the 4th and the 6th week of treatment and the 4th and 6th week in the period when placebo was given. At these intervals the clinical rating and psychological tests were performed. The EEG was computerized, the Fast fourier being used for analysis. The improvement of such symptoms as fatigue, memory impairment, decreased dynamogeny, emotional disorders, impairment of certain daily activities, and sleep impairment was statistically significant. Improvement was shown, as compared to placebo Ss, in reaction time but was less pronounced in immediate memory and attention (paired-associations, numeric square). In EEG there was a decrease in the amount of slow activity and the background rhythm became more regular. It is concluded that pyrithioxin is indicated in less deteriorated cases but at least several weeks of therapy are necessary to attain positive results. 22 references. (Journal abstract modified)

002725 Nino, R.; Iadevaia, F. M. G.; Sapio, M. Ospedale Psichiatrico Provinciale L. Bianchi, Naples, Italy /**Note 2: depression in the developmental age: clinicotherapeutic study of depression in the developmental age.**/ Nota II: La depressione

nell'eta evolutiva. (Contributo clinico-terapeutico allo studio della depressione nell'eta evolutiva). Ospedale Psichiatrico (Napoli). 44(1):69-94, 1976.

Clinical and therapeutic observations of ten children, 7 to 14 years old, suffering from depression are reported. EEG and metric tests such as Rorschach, TAT, CAT, and the Terman/Merril test were administered prior to the patients' being given 50 to 70mg of either imipramine or amitriptyline per day. After 15 days seven of the ten children showed marked improvement while the other three reacted only satisfactorily to the drugs. Results showed that depression does exist in children and can usually be diagnosed in children of about 8 years of age. Depression in children manifests itself in moodiness, apathy, anxiety, and guilt feelings. It is concluded that early diagnosis, use of all available psychometric tests, and correct use of appropriate drugs and psychotherapy can aid children in overcoming depression. 43 references.

002726 Pastrana, Elia. Departamento de Medicina Preventiva y Salud Mental, Comision Federal de Electricidad, Mexico City, Mexico **/Effects of Amitriptyline on the progress of depression./** Efectos de la amitriptilina en la evolucion de la depresion. Neurologia - Neurocirugia - Psiquiatria (Mexico City). 17(3):145-152, 1976.

Research on the evolution of symptoms of depressive syndromes of 33 subjects treated with amitriptyline compounds is presented. The drug was administered in oral dosage of 25mg once or twice daily. The doses were maintained for a minimum period of 8 weeks and a maximum of 14 weeks. Depressive syndromes showed improvement in 100 percent of the cases, with resolution of the clinical depression in 80 percent, according to psychiatric examinations, and psychological interviews. 17 references. (Journal abstract modified)

002727 Renard, P. no address **/Psychotherapeutic and chemotherapeutic relations in insomnia./** Relations psychotherapiques et chimiotherapiques dans les etats d'insomnie. Revue de Neuropsychiatrie de l'Ouest (Rennes). 14(54):61-72, 1976.

Insomnia in children and in adults and its psychotherapy and chemotherapy are examined. A number of techniques have been devised to treat insomnia: hypnosis, electrosleep, relaxation therapy derived from the autogenic training of Schulta, homeopathy, acupuncture, auriculotherapy, and chemotherapy (barbiturates, sedatives, hypnotics, antidepressants, and tranquilizers). The common characteristic in insomnia is anxiety. Barbiturates, for example, reduce anxiety by hypnotically inducing sleep, while tranquilizers reduce anxiety and promote sleep. The history and major trends in chemotherapy are reviewed. It is estimated that 2.5million French take some medication nightly to improve their sleep, of whom 95% have functional insomnia. Prevention of insomnia by sound family life, and improvement in social relationships, leading to a well balanced life, are recommended.

002728 Santos, Mario R.; Romi, Juan Carlos; Bertorello, Mario C. Clinica de San Jorge, Lanus, Provincia de Buenos Aires, Argentina **/Clinical evaluation of lorazepam in emergency psychiatry./** Evaluacion clinica del lorazepan en psiquiatria de urgencia. Neuropsiquiatria (Buenos Aires). 7(1):39-41, 1976.

A clinical evaluation of lorazepam in emergency psychiatric situations is presented. The objectives of the study were: 1) to evaluate the effectiveness of injectable lorazepam in the control of anxiety/agitation crises in neurotics with acute and serious profiles; 2) to evaluate local and systemic tolerance of parenterally administered lorazepam. Lorazepam was administered to 29 inpatients, 15 females and 14 males, average age of 49 years, who presented an anxiety crisis which called for a parenterally administered anxiolytic agent. Patients received an average parenteral dose of 6mglarazepam and were evaluated at intervals of 5, 10, and 30 minutes. The drug took effect within 5 minutes and the maximum effect was reached about 32.5minutes after the drug was administered. No intolerance or side effects were shown. The drug produced clear symptomatic improvement in all but 2 patients, both of whom exhibited psychotic anxiety.

002729 Sherman, David G.; Easton, J. Donald Division of Neurology, Southern Illinois University School of Medicine, Springfield, IL 62708 **Beta-adrenergic blockade and anxiety.** Lancet (London). No. 7991:911-912, 1976.

In a letter to the editor of Lancet, a case history of a 20-year-old man with a two year history of anxiety attacks is reported in whom isoproterenol hydrochloride failed to induce a typical anxiety attack, even though it produced a prominent tachycardia. A subsequent trial of oral propranolol, up to 320mg/day, brought no relief from the anxiety attacks. It is concluded that some anxious patients have relative beta-adrenergic hyperactivity, that they may be identifiable by the isoproterenol infusion test, and that they will probably benefit substantially from treatment with oral propranolol. 4 references.

002730 Somohano, Maria del Pilar; Broissin, Maria Cristina; Sobrino Z., Aimee. Servicio de Psiquiatria, Centro Femenil de Rehabilitacion Social, Mexico, D.F., Mexico **/Clinical evaluation of the effects of oxypertine in states of anxiety./** Valoracion clinica de los efectos de la Oxipertina en los estados de ansiedad. Neurologia - Neurocirugia - Psiquiatria (Mexico City). 17(3):171-180, 1976.

Oxypertine, a new anxiolytic drug related to the indolylazine compounds, was evaluated in a group of 30 legally confined female patients between the ages of 19 and 44 years most of whom presented severe acute and chronic anxiety. The methodology applied in this case was a modified double-blind randomized procedure. Patients were given a 10mg capsule every 12 hours. Anxiety was clinically measured using the Murphy Visual Anxiety Scale. For the nine patients who were treated with oxypertine for only 4 weeks, the response was excellent in 7 cases, fair in 1, and poor in 1. In the group that received the placebo for 4 weeks the response was excellent in 5, good in 1, and poor in 2. In another group which began with the placebo and which was changed to the active drug after 2 weeks because of stabilization or increase in the anxiety, the results were excellent in 3, good in 2, poor in 2, with one patient discontinuing treatment. In this same group, 6 cases started treatment with oxypertine and after 2 weeks or more were changed to the placebo for the same reasons. Results were fair in 1 and poor in 5 cases. A significant response was observed in those cases where oxypertine replaced the placebo and no response was obtained when the placebo substituted for the oxypertine. It is concluded that the administration of oxypertine at the dosage of 20mg to patients with severe anxiety provides little anxiolytic effect. 5 references. (Journal abstract modified)

002731 Suzman, M. M. 101 Tower Hill, Kotza Street, Hillbrown, Johannesburg, South Africa **Propranolol in the treatment of anxiety.** Postgraduate Medical Journal (Oxford). 52(Supplement 4):168-174, 1976.

The short-term and long-term results of beta-blockade with propranolol therapy in patients with anxiety syndromes, with or without depression, are presented. Of 725 patients presenting with anxiety syndromes, 513 were treated with propranolol for periods of several days to over 10 years, some intermittently, others virtually without interruption. Of these, 237 had previously received or were receiving psychotropic drugs, mostly benzodiazepines and/or phenothiazines, which had proved ineffective or deleterious. With few exceptions, the somatic and psychic symptoms were relieved or moderated and overall functional capacity was restored. Depression, evident in 50% of the patients, usually lifted, but persisted in one third as a long symptom responsive to antidepresssants. Propranolol requirements usually diminished and lasting remissions were not infrequent. It is concluded that effective control of the somatic and psychic symptoms of anxiety can be achieved with propranolol in appropriate dosage. 29 references. (Author abstract modified)

002732 Toru, Michio; Moriya, Hirofumi; Yamamoto, Kosei; Shimazono, Yasuo; Ishiguro, Takeo; Sugano, Keiju; Isse, Kunihiro; Miyasaka, Matsue. Department of Neuropsychiatry, School of Medicine, Tokyo Medical and Dental University, Tokyo, Japan **A double-blind comparison of sulpiride with chlordiazepoxide in neurosis.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 30(2):153-164, 1976.

The therapeutic effectiveness of sulpiride on various types of neurosis was compared with that of chlordiazepoxide on a double-blind basis. The subjects consisted of 41 males and 32 females. The rate of global improvement was 79% for the sulpiride group and 90% for chlordiazepoxide group. Improvement by manifestation and type of neurosis also matched. Side-effects occurred at a rate of 28% (sulpiride group) and 30% (chlordiazepoxide group), and also matched closely in incidence and variety. It is concluded that sulpiride in appropriate doses is useful in the treatment of neurosis without causing extrapyramidal side-effects. 11 references. (Author abstract modified)

002733 Turner, Paul. Department of Clinical Pharmacology, St. Bartholomew's Hospital, London, England **Clinical and experimental studies on the effects of propranolol in anxiety.** In: Carlsson, C., Neuro-hsychiatric effects of adrenergic beta-receptor. Munich, Urban & Schwarzenburg, 1976. 120 p. (p. 61-64).

In a paper presented at a symposium on neuropsychiatric effects of adrenergic beta-receptor blocking agents held at Copenhagen, October 1975, numerous controlled studies are cited showing that the action of propranolol in the relief of anxiety tends to be primarily somatic. The results are interpreted as suggesting that beta-adrenoceptor blockade is important in the therapeutic effect of these drugs in anxiety, and that a peripheral nervous system rather than a central nervous system mechanism is probably involved. 13 references.

002734 Vella, Gaspare; Tatarelli, Roberto. Universita di Roma, II Clinica Psichiatrica, Rome, Italy **/Anxiety, restlessness and anxiolytics./** Ansia, ansiosi e ansiolitici. Rivista di Psichiatria (Roma). 11(6):463-499, 1976.

Anxiety is defined from various points of view and various levels of analysis, and a critical review of the drug therapy of anxiety is presented, focusing on present abuse and therapeutic misuse of drugs. Problems discussed include: 1) clinical classification of hypnotic/sedative antianxiety drugs such as barbiturates, meprobamate, and benzodiazepine; 2) use of other drugs identified as sedative/vegetative, such as hydroxine and diphenhydramine, which affect the nervous system; 3) relevance of nondrug factors, and drug side-effects and toxicity; and 4) drug dependence, suicide, and aggressive behavior. An historical overview of the drug boom during the past 20 years also is presented, with particular emphasis on antianxiety drugs and their easy acquisition. It is suggested that better methods of distribution and control be effected, that better diagnositc methods be developed, and that the psychotherapeutic rapport among physician, pill, and patient be enhanced. 154 references.

002735 Yensen, Richard. University of California, Irvine, CA **The use of 3,4-methylenedioxyamphetamine (MDA) as an adjunct to brief intensive psychotherapy with neurotic outpatients. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-7258 HC$20.00 MF$10.00 233 p.

Ten neurotic outpatients were treated with brief intensive psychotherapy assisted with 3,4-methylenedioxyamphetamine (MDA). The drug was used as psychoadjuvant in the context of a preestablished therapeutic relationship. MDA was given in a specially designed setting in doses ranging from 75-200mg. MDA was found to produce a range of effects, in this setting, from enhanced introspection with moderately increased emotionality to visual imagery and intense emotional expression. A significant reduction in test scores measuring depression, anxiety, obsessive-compulsive traits, and hysterical tendencies was observed immediately after therapy. Significant increases in measures of well-being and self-actualization were found. The beneficial results were, on the whole, stable during the 6 month follow-up period. (Journal abstract modified)

11 DRUG TRIALS IN MISCELLANEOUS DIAGNOSTIC GROUPS

002736 Agrell, Berit; Dehlin, Ove; Falkheden, Thomas; Nordqvist, Percy. Langvardskliniken, Centrallasarettet, Molndal, Sweden. **/Hypnotic effects of dixyrazine in a double-blind crossover study on geriatric patients./** Provning av dixyrazin som hypnotikum till geriatriska patienter: en dubbel-blind "cross-over" studie med dixyrazin, nitrozepam och placebo. Nordisk Psykiatrisk Tidsskrift (Kungsbacka). 30(5):377-383, 1976.

Hypnotic effects of dixyrazine on geriatric patients average age 77.5years was studied in a double-blind crossover comparison with nitrazepam and placebo. Dosages of 25mg dixyrazine, 5mg nitrazepam, and placebo were given at bedtime for three weeks. Registered variables were: 1) length of time until falling asleep; 2) number of times of waking up during the night; 3) condition of the patient at 6 AM. The length of time until falling asleep was significantly shorter for both dixyrazine and nitrazepam compared to placebo. The number of times of waking up during the night was lower for dixyrazine and nitrazepam compared to placebo. At 6 AM the number of patients still asleep was higher when treated with dixyrazine compared to nitrazepam and placebo. The study shows that dixyrazine is an effective alternative to other hypnotic drugs for geriatric patients. 7 references.

002737 Allen, Harry E.; Dinitz, Simon; Foster, Thomas W.; Goldman, Harold; Lindner, Lewis A. Ohio State University, Columbus, OH 43210 **Sociopathy: an experiment in internal environmental control.** American Behavioral Scientist. 20(2):215-226, 1976.

An assessment of a treatment program for offenders diagnosed as simple sociopathic types which employed a variety of

readily available and widely used compounds in an experimental format was presented. The program was instituted under the direction of the Ohio Department of Rehabilitation and Correction. In all 41 men diagnosed as antisocial sociopaths agreed to cooperate for a 6 month period of drug treatment. Offenders were tested and immediately placed on placebo medication for a period of 1 month, after which they received imipramine hydrochloride (pamoate) for 3 months, followed by a final placebo period of 2 months; a subgroup received placebo only during this period. The medication, both drug and placebo, was delivered to the institution in individual marked containers and dispensed twice from the institution's pill center. Patient's dosages were regulated using a symptom checklist that was administered twice weekly as well as daily verbal reports and monthy EKGs. Such monitoring enabled the titration of dosage to avoid such side-effects as profuse sweating, the most consistently reported discomfort. The results of this study indicate that pamoate is able to reduce at least the grosser behavioral symptoms associated with this chronic antisocial personality syndrome. 22 references.

002738 Ananth, J.; Sangani, H.; Noonan, J. P. A. Department of Psychiatric Education and Research, St. Mary's Hospital, Montreal, P. Q., Canada **Amantadine therapy for drug-induced extrapyramidal signs and depression.** Psychiatric Journal of the University of Ottawa (Ottawa). 1(1-2):27-30, 1976.

In a controlled comparative study of 45 patients manifesting drug induced extrapyramidal signs, randomly selected groups of 15 patients each received amantadine, ethopropazine, or benztropine for 2 weeks. All patients had both a psychiatric and a neurological examination. The Brief Psychiatric Rating Scale and the Extrapyramidal Symptom Rating Scale were completed in the beginning and on the first, fourth, seventh, and fourteenth day of the study. Results indicate amantadine to be both a safe and effective antiparkinsonian agent. The lack of anticholinergic side-effects makes its use particularly relevant. Findings suggest that amantadine may be useful in treating some depressed patients. 9 references. (Author abstract modified)

002739 Atsmon, Abraham. Gehah Psychiatric Hospital, Beilinson Medical Center, Petah Tiqva, Israel **Early observations of the effect of propranolol on psychotic patients.** In: Carlsson, C., Neuro-psychiatric effects of adrenergic beta-receptor. Munich, Urban & Schwarzenburg, 1976. 120 p. (p. 86-90).

In a paper presented to a symposium on neuropsychiatric effects of adrenergic beta-receptor blocking agents held at Copenhagen, October 1975, the results of a trial of propranolol on patients exhibiting a specific symptom complex, regardless of diagnosis, are reported. The symptom complex included increased psychomotor activity, marked tension, disturbances in thought processes and affect, and hallucinations. Propranolol was administered every 3 to 4 hours around the clock, and the dosage was determined by pulse rate and/ or blood pressure only; the customary 160mg per day maximum was disregarded unless side-effects dictated otherwise. The following observations were made: 1) the therapeutic dose of propranolol showed very marked individual variation; 2) improvement of the psychotic symptoms was always slightly preceded or accompanied by a lowering of the pulse rate and of the blood pressure; 3) several patients experienced a toxic psychosis, characterized by delirium and visual hallucinations; and 4) in several patients, blood pressure rose on days when an increase in the dose of propranolol caused the pulse rate to drop to 58 to 60 per minute. Generally, however, the drug effects were found to be positive.

002740 Badiche, A.; Joubrel, J.-P. C.H.S.P., 108, avenue du General-Leclerc, F-35011 Rennes Cedex, France **/Importance of Promotil in followup treatment of alcoholics./** Interet du Promotil dans le traitement post-cure des alcooliques. Revue de Neuropsychiatrie de l'Ouest (Rennes). 14(51):37-41,43-48, 1976.

The role of Promotil (phenyl-l-pyrrolidino-2-pentane HCl) in the followup treatment of alcoholics was examined in 45 patients. Of these, 12 patients received promotil alone, 17 received Promotil in combination with diazepam, 7 were given Promotil with an antidepressant, and 9 received Promotil with Esperal. The study covered 1 year. Results showed 42% of patients did not relapse, 22% returned to alcoholism, and 36% showed uncertain behavior. Results showed Promotil has definite antiasthenic action, diminishes fatigability, and stimulates libido, which for the most part correspond to the demands of the alcoholic. Despite an orexigenic effect, no significant weight change was noted. It is concluded that Promotil greatly favors contact with the psychotherapist and is an effective and valuable medication in alcoholism.

002741 Bellak, Leopold; Karasu, Toksoz B.; Birenbaum, Caroline. Albert Einstein College of Medicine, 1300 Morris Park Ave., Bronx, NY 10461 **Geriatric psychiatry: a handbook for psychiatrists and primary care physicians.** New York, Grune and Stratton, 1976. 320 p. $15.00.

A basic handbook of geriatric psychiatry intended for psychiatrists and psychiatric residents and to provide useful information for any care giving professionals working with the aged is presented. A broad scope includes such subject areas as: 1) depression; 2) both individual and group psychotherapy with the elderly; 3) personality changes with aging; 4) cognitive deficits; 5) neuropsychiatric disorders; 6) mental status examinations; 7) sexual decline and impotence; 8) urological disorders; 9) socioeconomic aspects in old age; 10) societal attitudes, aged stereotypes, and professional bias toward the elderly; 11) social agencies; 12) psychopharmacology with the aged; 13) comprehensive care including daycare, community care, and institutional care; 14) crisis intervention; 15) legal aid; 16) health benefits including Medicare and Medicaid; and 17) terminal patient management and family bereavement. Appendices contain lists of government provisions for the elderly including low-income elderly programs and volunteer/employment programs, and organizations pertaining to the aged.

002742 Blachly, Paul H. no address **Naloxone in opiate addiction.** Current Psychiatric Therapies. 16:209-213, 1976.

The use of the opiate antagonist naloxone in treatment and rehabilitation of opiate addicts is described. Naloxone is seen as useful in three aspects of treatment and rehabilitation: 1) diagnosing physical dependence; 2) indicating opiate use in opiate abstinence treatment programs; and 3) abruptly detoxifying opiate addicts. In diagnosis, entry of nonaddicted clients and refusal of addicted clients due to unreliability of patients' testimony and urinalyses may be prevented. Abrupt detoxification with increasing doses of naloxone is described; ketamine was used to relieve discomfort. It is concluded that in such a program major problems occur after the patient leaves the hospital; delayed abstinence syndrome may cause dysphoria, insomnia, and restlessness. Tendencies to seek relief in alcohol, tranquilizers, and sleeping pills; and episodes of depression are seen as requiring firm, sympathetic medical and social management. 10 references. (Author abstract modified)

002743 Blitt, C. D. no address **Lorazepam is a satisfactory preanaesthetic sedative if used with care.** Anesthesia and Analgesia. 55:522, 1976.

Lorazepam, an extremely potent and satisfactory preanaesthetic sedative with amnesic properties, is considered to be acceptable and well tolerated by patients. Care must be taken not to give too much and it is not recommended as premedication for outpatients. In 50 patients 4mg lorazepam IV given 1 hour after 50mg IM meperidine and 0.6mg IM atropine was associated with 85% amnesia compared with 5% in the placebo group. Two patients exhibited disorientation and hallucinatory behavior with lorazepam. There does not appear to be a correlation between plasma concentration of lorazepam and lack of recall. In 50 patients 4mg lorazepam and 100mg pentobarbitone both given IM as the sole premedicant did not differ significantly in sedative effect or acceptability. However, there was 68% amnesia in the lorazepam group compared with 16% in the pentobarbitone. Drowsiness in 40 patients occurred sooner (6.9min) with lorazepam bolus than IV continous drip (8.15 min mean). Euphoria occurred in one patient and hallucinations in another. (Author abstract)

002744 Boller, Francois. Neurobehavior Unit, Cleveland Veterans Administration Hospital, Cleveland, OH 44106 **Treatment of nightmares.** Medical Journal of Australia (Glebe). 2(14):548, 1976.

In a letter to the editor, the possible treatment of Feldman's patients (those who have nightmares that might be properly called night terror) with propranolol is discussed. This type of nightmares includes ordinary but terrifying dreams which elicit an elaborate recall of content, can be seen at all ages, and occur during rapid eye movement (REM) sleep. Animal studies have suggested that the maintenance of REM sleep depends on pontine noradrenergic mechanisms located in the regional of the locus ceruleus. It would therefore appear at least plausible that the symptomatic relief experienced by Feldman's patients after propranolol may be secondary to a decrease in REM sleep. However, it would be inappropriate to treat children suffering from the type of nightmare which is accompanied by great anxiety but little recall and occurs during nonrapid eye movement (NREM) sleep with beta-adrenoreceptor antagonists. 3 references.

002745 Bukowczyk, Adam; Wasik, August; Brys, Jozef; Horodnicki, Jan; Szydlik, Henryk; Domagalski, Jerzy. Klinika Psychiatryczna, Akademia Medyczna, Wroclaw, Poland **/Clinical evaluation of nitrazepam-Polfa./** Ocena kliniczna nitrazepamu-Polfa. Psychofarmakoterapia Schizofrenii Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 177-182).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, a clinical evaluation of nitrazepam (Neozepam-Polfa) in schizophrenics and depressives is presented. Neozepam-Polfa is a tranquilizing agent acting on the nervous system and on psychic disturbances, and is effective in overcoming insomnia. The data presented indicate that in addition to its psychotropic action, the drug is most effective in suppressing neuroleptic side-effects.

002746 Carini, A.; Ferrazzi, D.; Ottavio, L.; Perosino, N. Istituto Ospedaliero Provinciale, Paolo Pini, Milan, Italy **/Experience in the use of delayed action drugs in the prevention of delirious psychoses./** Esperienza sull'impiego di farmaci ad azione ritardata nell'ambito della profilassi delle psicosi deliranti. Igiene Mentale (Trapani). 20(2/3):349-363, 1976.

Paper presented at the 10th National Congress of the Italian Mental Hygiene Society, Milan, 1975, describes the use of fluphenazine decanoate with 57 patients with delirious psychoses, showing the drug's positive effect on delirium and subsequent behavior. Of 100 female patients administered the drug over a 6 month to 2 year period in the women's ward of the Paolo Pini Psychiatric Institute in Milan, 57 reported psychic disturbances, including schizophrenia, chronic delirium, chronic hallucinatory delirium, acute delirium and borderline personality. Results show the drug was well tolerated by all patients, regardless of age, and that during a year followup observation only 10 patients reported delirious recurrences of significance. It is concluded that fluphenazine decanoate may be considered one of the most valuable drugs in secondary and tertiary prevention of delirious psychoses. 19 references.

002747 Coper, H.; Kanowski, S. Institut fur Neuropsychopharmakologie der Freien Universitat, Ulmenallee 30, D-1000 Berlin 19, Germany **/Geriatric drugs: theoretical foundations, expectations, control, and criticism./** Geriatrika: theoretische Grundlagen, Erwartungen, Prufung, Kritik. Hippokrates (Stuttgart). 47(4):303-319, 1976.

The efficacy of drugs used in the treatment of geriatric conditions was investigated from theoretical and clinical perspectives. Prophylactic and therapeutic expectations attached to so called geriatric drugs have not been stated with sufficient clarity to permit controlled research. Past studies have addressed cellular and molecular changes during the aging process while neglecting the functional impairment of the total organism. The redundancy of CNS regulatory mechanisms suggests that the organism may retain normal limits despite the loss of partial capacity. Geriatric drugs are expected to stabilize functional systems and prevent their homeostatic disengagement. Psychovegetative support of older patients through medication is complicated by unpredictable metabolic reactions with respect to water, electrolyte, and heat exchange, and observation of biochemical effects is frequently obstructed by multiple disease processes, nonspecificity, interference, sensory impairment, and the heterogeneity of the clinical sample. Objective measurement is, moreover, vitiated by unpredictable mood changes, motivational peculiarities, and hypochondria in geriatric patients. Additional variables are introduced by the social and therapeutic environment. A seven point program for scientific investigation of geriatric drugs is proposed. Judged by the standards of this program, procaine, substances with encephalotropic action, RNA stimulants, and cerebral blood flow enhancers do not meet the desired criteria. 56 references.

002748 Cwynar, Stanislaw; Napieralska, Miroslawa; Posel, Zbigniew; Siuchninska, Helena; Tomczak, Wojciech; Wojdyslawska, Irena. Klinika Psychiatryczna, Akademia Medyczna, Lodz, Poland **/Use of thioridazine-retard in psychiatric treatment./** Zastosowanie thioridazin-retard w lecznictwie psychiatrycznym. Psychofarmakoterapia Schizofrenii Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 225-228).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, the use of thioridazine retard in psychiatric treatment is presented. The drug was given to 51 schizophrenic and depressive patients at the Lodz Psychiatric Clinic, of whom 82% were schizophrenic. All patients had previously been treated with neuroleptics and some had been given insulin and electric shock treatment. The drug proved to be effective in 72% of the cases, with only one patient showing negative results. It is concluded that thioridazine retard is

an effective drug for treating schizophrenia and depression and convenient to administer and control.

002749 Dalby, Mogens A. Department of Neurology, University of Aarhus, Municipal Hospital, Aarhus, Denmark **The effect of propranolol in stammering.** In: Carlsson, C., Neuropsychiatric effects of adrenergic beta-receptor. Munich, Urban & Schwarzenburg, 1976. 120 p. (p. 72-73).

In a paper presented to a symposium on neuropsychiatric effects of adrenergic beta-receptor blocking agents held at Copenhagen, October 1975, the conflicting results of two studies testing the effect of propranolol on stammering are reported. The first study was informal, including three adults and four children. Five persons showed marked improvement within a week. The second study was a formal, double-blind crossover which included 26 persons and lasted 12 weeks; here the efficacy of propranolol over placebo was found to be nil. No conclusion can be reached, except to say that a beneficial effect of propranolol on stammering has not been proved. It is asserted, however, that the observations from the first study seem so compelling that further studies are strongly indicated. 3 references.

002750 Delvaux, V.; Taziaux, P.; Devroye, Y. Vaux-sous-Chevremont, Universite de Liege, Chenee, Liege, France /**A double-blind comparison of a new hypnotic, flunitrazepam (Ro 5-4200), with a barbiturate.**/ Comparaison selon la methode double insu d'un nouvel hypnotique, le flunitrazepam (Ro 5-4200) avec un barbiturique. Revue Medicale de Liege (Bruxelles). 31(16):485-490, 1976.

A two phase investigation of flunitrazepam (Ro 5-4200) as compared to barbiturates in the management of insomniacs is reported. The first phase was a short-term, double-blind comparison of flunitrazepam, phenobarbital, and a placebo in 80 insomniac patients; the second phase was an uncontrolled, long-term (12 mo) followup of flunitrazepam in 96 insomniacs. The results of Phase 1 indicated that flunitrazepam was more effective than phenobarbital or placebo in the management of insomnia as measured by rate of inducing sleep, the duration and quality of the induced sleep, and the subject's state upon awakening (refreshed or somnolent). The results of Phase 2 indicated that the initial favorable results with flunitrazepam in insomniacs did not deteriorate with repeated dosages over time and was preferred over previous barbiturate medications by 76% of the subjects. It was concluded that flunitrazepam was superior to barbiturates for the management of insomniac patients. 15 references.

002751 Dowzenko, Anatol. 6B Zloczowska, Warsaw 03-972, Poland /**Attempt at treating Parkinsonism with agonists of the dopaminergic system.**/ Proby leczenia Parkinsonizmu anagonistami ukladu dopaminergicznego. Neurologia i Neurochirurgia Polska (Warszawa). 10(4):579-582, 1976.

Attempts at treatment of Parkinsonism with agonists of the dopaminergic system have developed as a natural outgrowth of the breakthroughs achieved with L-dopa. Of several similar drugs developed through this process 2-bromo-alpha-ergokryptene known as Bkr appears to have therapeutic possibilities. Experiments with these drugs are discussed, and the dosage and related side-effects are listed. It is concluded that BKr can be an effective substitute or adjunct for use in some patients, in that it is equally effective, while possessing different side-effects. 11 references.

002752 Dugas, M.; Grenet, P.; Masson, M; Mialet, J. P.; Jaquet, G. Hopital Herold, 4, place Rhin-et-Danube, F-75935 Paris Cedex 19, France /**Aphasia in a child with epilepsy: improvement under antiepileptic treatment.**/ Aphasie de l'enfant avec epilepsie: evolution regressive sous traitement antiepileptique. Revue Neurologique (Paris). 132(7):489-493, 1976.

A case report is given of aphasia associated with epilepsy in a female child. Frequent epileptic episodes of various forms first occurred at 5, and at age 8, aphasic problems in written language appeared. At age 9, a severe aphasia appeared, predominantly expressive, with lack of words, paraphasia, and dyssyntaxia. Her IQ was 107. EEG showed many abnormalities, but brain scan and carotid arteriography were normal. Treatment was begun with 100mg phenobarbital, which led to rapid improvement with regard to epileptic crises and a marked improvement in language; however, there was still a mild residuum of the aphasia. 7 references.

002753 Dupont, Erik. Department of Neurology, University of Aarhus, Municipal Hospital, Aarhus, Denmark **The effect of beta-adrenergic blockade (propranolol) on different tremors.** In: Carlsson, C., Neuro-psychiatric effects of adrenergic beta-receptor. Munich, Urban & Schwarzenburg, 1976. 120 p. (p. 65-71).

In a paper presented at a symposium on neuropsychiatric effects of adrenergic beta-receptor blocking agents held at Copenhagen, October 1975, the results of a double-blind crossover study testing the efficacy of propranolol versus placebo in the treatment of benign essential tremor, some associated with psychiatric disorders, are reported. Patients who were first given propranolol showed significantly better results in all parameters during the propranolol treatment period. In contrast, the patients who were first given placebo showed no significant difference between the placebo and propranolol treatment period. The findings were interpreted as showing that the effect of propranolol in the given doses is of about the same magnitude as the placebo effect; however, it is a durable effect which remained unchanged over the period of the study, whereas the effect of placebo faded off. Generally, the beneficial effects of propranolol were shown to be more pronounced in the younger subjects. 30 references.

002754 Floru, L.; Brosteanu, E.; Schink, P. Rhenania District Hospital, Psychiatric University Clinic, Dusseldorf, Germany **Double-blind study of the effect of propranolol against placebo in the withdrawal syndrome of alcoholics, hypnotics, tranquilizers, analgetics, and opiates -- a preliminary report.** In: Carlsson, C., Neuro-psychiatric effects of adrenergic beta-receptor. Munich, Urban & Schwarzenburg, 1976. 120 p. (p. 43-44).

In a paper presented at a symposium on neuropsychiatric effects of adrenergic beta-receptor blocking agents held in Copenhagen, October 1975, it is reported that 40 female alcoholic and drug patients underwent a double-blind study to determine the relative merits of propranolol versus placebo in the withdrawal syndrome. Day 3 results for those on the propranolol regimen included one delirium, 12 good improvements, 6 moderate improvements, and 1 patient very slightly changed. Day 3 results for the patients on the placebo regimen included 1 delirium, 9 moderate improvements, 9 very slight improvements, and 1 worsened patient. It is concluded the use of propranolol had an obviously positive effect with respect to EEG readings, the psychogalvanic test, and respiratory amplitude, but that it is not possible to state a significantly positive effect of propranolol with respect to delirium.

002755 Franzen, Goran. Forskningsavd. S:t Lars sjukhus, S-220 06 Lund, Sweden /**Anticonvulsant therapy for epilepsy by**

determination of plasma concentrations./ Antikonvulsiv terapi vid epilepsi. Nagra enfarenheter av serumkoncentrationsbestamningar av antiepileptiska farmaka. Nordisk Psykiatrisk Tidsskrift (Kungsbacka). 30(1):3-13, 1976.

Anticonvulsant therapy by determination of plasma concentrations is described. The study, carried out between 1972 and 1974, included 100 epileptic patients where 1/3 had not had any seizures that last 3 years, 1/3 had seizures once a month and the rest of the patients had epileptic seizures more frequently. Treatment with barbiturates has decreased, being more and more substituted by phenytoin, while treatment with carbamazepine has been constant. Serum concentrations of phenytoin were below 10microgram/ml for 25 of 41 patients, and the frequency of grand mal seizures for these 25 patients averaged 14 per year. By increasing the dose of phenytoin from 3.9mg/kg bodyweight to 5.2mg/kg, the frequency of grand mal seizures decreased by 60%. The frequency of seizures also decreased, averaging from 18 to 13 seizures per year. An adjustment of the therapeutic serum levels of carbamazepine and barbiturates did not change the seizure frequency significantly. Nine patients receiving 6 to 30mg diazepam per day, in addition to the usual antiepileptics, required larger doses of phenytoin to reach the therapeutic serum level where the frequency of seizures decreased. 29 references.

002756 Fumi, S.; Bertoletti, P.; Opice, B. Ospedale Psichiatrico Santa Maria della Pieta, Rome, Italy **/Clinical experiences with fluphenazine decanoate (DF) in 50 long-term patients./** Esperienze cliniche con decanoato di flufenazina (D.F.) su 50 pazienti lungodegenti. Clinica Psichiatrica (Roma). 12(20):151-155, 1976.

The use of fluphenazine (DF) decanoate as a long-acting drug is described along with its positive and negative effects. DF was administered to 50 patients with epilepsy, schizophrenia, or mental deficiency for at least 10 years standing. Collateral effects were seen in only 14 patients. Conclusive results show that DF is long-acting, is especially useful with outpatients, and that it has promise as being an ideal drug for mental patients who must have psychopharmacotherapy. 6 references.

002757 Grosz, Hanus J. Institute of Psychiatric Research, Indiana Univ. School of Medicine, 1100 West Michigan, Indianapolis, IN 46202 **Current state of research on propranolol-opiate interaction.** In: Carlsson, C., Neuro-psychiatric effects of adrenergic beta-receptor. Munich, Urban & Schwarzenburg, 1976. 120 p. (p. 36-42).

In a paper presented at a symposium on neuropsychiatric effects of adrenergic beta-receptor blocking agents held in Copenhagen, October 1975, investigations of the interaction between propranolol and the opiates in both man and animals are reviewed. The results of the various investigations are seen as contradictory and inconclusive. It is speculated that one possible reason for the reported discrepancies may be related to mode and sequence of drug administration. In a 1975 study in which 85 physically healthy heroin addicts were treated with propranolol, the results were seen as disappointing. 20 references.

002758 Guthy, Heinrich. Nordallee 1, D-5500 Trier, Germany **/On the therapy of withdrawal symptoms in chronic alcoholism with oxazepam./** Zur Therapie von Entzugserscheinungen bei chronischem Alkoholismus mit Adumbran. Therapie der Gegenwart (Munchen). 115(8):1365-1372, 1976.

The effect of oxazepam on withdrawal symptoms in chronic alcoholism was studied in 48 male alcoholics between 20 and 61 years of age, who had been alcoholic for 1 to 16 years. Patients began with a dose of 100mg/day oxazepam, which was adjusted individually as treatment progressed. The patients, who were hospitalized, were observed for 6 weeks. Improvement was observed in nearly all patients in anxiety, irritability, excitement, sleep disturbances, tremor, and perspiration, with therapy being judged successful in 45 of 48 patients. There was significant improvement in body weight, hemoglobin, and liver function tests. 14 references.

002759 Hachijima, Yuko; Ishishita, Kyoko. Department of Psychiatry, Fukushima Medical University, Fukushima, Japan **The therapy and course of autism.** Psychiatria et Neurolgia Japonica (Tokyo). 78(8):575, 1976

In a paper read at the 30th Northern Japan Psychoneurological Symposium held in September 1975 at the New Grand Hotel in Akita, Japan, a report was given on the therapy of 8 children who had been diagnosed as having Kanner's early infantile autism, and in whom organic brain damage could not be ruled out. Along with isolation, hyperactivity, and emotional instability were noted. An average of .039mg/kg/day of haloperidol was administered, which helped reduce hyperactivity and autistic, speech impediments, and cognitive disorders of the children so that some could be removed from special classes and put into normal ones. Special treatment for these children, however, was still thought to be needed.

002760 Herrmann, W. M.; Beach, R. C. Klinische Forschung Neuropsychopharmakologie, Schering AG., Postfach 6503M, D-1000 Berlin 65, Germany **Psychotropic effects of androgens: a review of clinical observations and new human experimental findings.** Pharmakopsychiatrie Neuro-Psychopharmakologie (Stuttgart). 9(5):205-219, 1976.

The pharmacological effects of androgens on behavior are reviewed, based on the clinical and experimental literature. Clinical findings are discussed concerning behavioral effects of androgen deficiencies, androgen excess, and androgen therapy. Clinically, androgens seem to have psychostimulant and psychoenergizing properties, and they influence sexual behavior when given to certain patients with androgen deficiency. The experimental literature is reviewed concerning the biochemical, electrophysiological, and experimental psychological findings on the effects of androgens. Androgens have an effect on sexuality, aggression, energy level, psychomotor function, higher mental performance, depression, and personality characteristics. 54 references.

002761 Ifabumuyi, O. I.; Jeffries, J. J. London Psychiatric Hospital, London, Ontario, Canada **Treatment of drug-induced psychosis with diphenylhydantoin.** Canadian Psychiatric Association Journal (Ottawa). 21(8):565-569, 1976.

An alternative to the major tranquilizers in the treatment of acute psychotic breakdown following multiple drug abuse, diphenylhydantoin, is introduced. The patients described had been taking hallucinogenic drugs for over 5 years, but only three of several successfully treated cases are described. In two of these cases EEG recordings did not show any localized epileptiform activity. The response to diphenylhydantoin is described both clinically and as recorded by EEG. An initial 2 week period is necessary in order that the effects of the drugs can be demonstrated clinically or on EEG tracing. It cannot be concluded from this that the antiepileptic drugs are the drugs of choice in drug induced psychosis; but, diphenylhydantoin has shown dramatic effectiveness in these previously refracto-

ry cases. In view of the response, some abnormal cerebral discharge from an as yet undiscovered locus may be involved in the pathogeneis of drug induced hallucinations. 12 references. (Author abstract modified)

002762 Ignatowicz, Roman; Jaremko, Aleksander. Panstwowej Sanatorium Neuropsychiatrii Dziecicecej, Nowyj Czarnow, Poland **/Observations on the use of amizepine on children with minimal central nervous system dysfunctions./** Spostrzezenia nad stosowaniem amizepiny u dzieci z minimaln dysfunkcja osrodkowego ukladu nerwowego. Psychofarmakoterapia Schizofrenii Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 221-224).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, observations on the use of amizepine, the Polish version of Tegretal, on children with minimal central nervous system dysfunctions are presented. The drug was given to 41 children divided into 2 groups according to their symptom classification. Results show that amizepine was very effective in this application and that side-effects were rare. 11 references.

002763 Ishishita, Kyoko; Hachijima, Yuko. Department of Psychiatry, Fukushima Medical University, Fukushima, Japan **Therapy for hyperactivity seen in minimal brain dysfunction.** Psychiatria et Neurologia Japonica (Tokyo). 78(8):574-575, 1976.

In a paper given at the 30th Northern Japan Psychoneurological Symposium held in September 1975 at Akita, Japan, 11 children aged 7 to 11 with learning disabilities thought to be due to minimal brain dysfunction (MBD) are evaluated. These children moved excessively, were cranky, and had difficulty in maintaining their attention span, but scored an average of 142 on the WISC IQ test. Their bad marks in school particularly in the subjects of Japanese language, music, and physical education. This was thought due to the minor neurological signs of MBD (i.e.,clumsiness, visual/cognitive abnormalities). This was very effectively treated by the administration of .02 to .03mg/kg/day of haloperidol, sometimes used for epileptics and the mentally retarded. They eventually overcame all of their symptoms of hyperactivity, clumsiness, and visual/cognitive disorders, and their school performance improved.

002764 Johnson, Bertha C. A. Yaba Psychiatric Centre, Lagos, Nigeria **Mental disorders other than schizophrenia and depression.** In: Advances in the drug therapy of mental illness. Geneva, World Health Organization, 1976. 168 p. (p. 83-91).

Drug treatment for mental disorders other than schizophrenia and depression is briefly reviewed. Examples are used from the following areas: neurotic disorders, psychosomatic disorders, child psychiatry, psychiatric states associated with abuse of alcohol and drugs, psychoses or behavioral disorders associated with epilepsy, psychoses associated with organic brain disorder, and iatrogenic effects. The ability of psychopharmacotherapy to make a real contribution to the overall treatment of mental disorders is discussed.

002765 Karasu, Toksoz B.; Murkofsky, Charles A. Albert Einstein College of Medicine, 1300 Morris Park Ave., Bronx, NY 10461 **Psychopharmacology of the elderly.** In: Bellak, L., Geriatric psychiatry. New York, Grune & Stratton, 1976. 320 p. (p. 225-244).

The relevant issues regarding psychopharmacology of the elderly are discussed in order to provide a framework for psychopharmacological treatment of the elderly. Studies of metabolic handling of drugs in the aged indicate the need for caution in prescribing drugs so as to avoid overdosing. The most important psychological issue in drug management in the aged is sensitivity to the placebo potential (positive and negative) of pharmacological treatment. Prescribing dosages of psychotropic medications in the elderly requires an awareness of the drug's significant action time as well as an awareness of the anticholinergic syndrome which results from adverse effects of psychotropic drugs. The few symptoms specifically amenable to pharmacologic intervention include treating a few target phenomena, which include anxiety, insomnia, agitation, psychotic behavior, schizophrenia and similar syndromes, depressive syndrome, mania and manic like symptoms. The typical geriatric patient has a clinical presentation that combines several major symptoms which vary in proportion and degree, making diagnosis difficult. Combination symptomatology often calls for the use of more than one drug, and the clinician should decide which of the multiple targeted symptoms demands priority. The interaction of various drugs, such as minor tranquilizers, neuroleptics, monoamine oxidase inhibitors, tricyclics, and lithium carbonate, is discussed. 15 references.

002766 Keup, Wolfram. Karl-Bonhoeffer-Nervenklinic, Berlin, Germany **The use of beta-blockade in dependence.** In: Carlsson, C., Neuro-psychiatric effects of adrenergic beta-receptor. Munich, Urban & Schwarzenburg, 1976. 120 p. (p. 58-60).

In a paper presented at a symposium on neuropsychiatric effects of adrenergic beta-receptor blocking agents held in Copenhagen, October 1975, the results of a double-blind study, comparing the effect of propranolol to that of placebo in alcoholics as well as opiate addicts on their subjective and objective withdrawal symptoms as well as their specific hunger for the substances abused are reported. The data show that propranolol was able to produce favorable results more often than placebo, but that placebo also was able to improve some patients profoundly. Tremor, heart frequency, perspiration, and anxiety were the symptoms best improved, but a drop in blood pressure became at times a limiting factor with regard to any further increase in dosage. It is concluded that propranolol is capable of influencing the withdrawal symptoms of alcoholics to some degree, but that in opiate dependents this influence was both less pronounced and inconsistent.

002767 Kupietz, Samuel S.; Balka, Elinor B. Child Psychiatric Evaluation Research Unit, New York State Department of Mental Hygiene, 524 Clarskon Avenue, Brooklyn, NY 11203 **Alterations in the vigilance performance of children receiving amitriptyline and methylphenidate pharmacotherapy.** Psychopharmacology (Berlin). 50(1):29-33, 1976.

The effects of amitriphytline (Elavil) and methylphenidate (Ritalin) on the vigilance of 20 hyperactive, aggressive children was investigated using an auditory version of the Continuous Performance Test (CPT). Over the course of this letter detection task, correct detections tended to return to pretreatment levels under placebo, but were maintained at significantly improved levels under Elavil and Ritalin. The relatively steep performance decrement which occurred in the placebo condition was found to be associated with a progressive increase in responses to the letter which immediately followed a target letter. Treating these late responses as slow but correct detections failed to eliminate the treatment effects obtained with

Elavil and Ritalin. It was concluded that in addition to keeping detection response latencies from increasing, the medications produced a heightened level of vigilance which resulted in an absolute increase in the number of correct detections. Findings suggested that children's ability to process information was unaffected by the reported side effect. 16 references. (Author abstract modified)

002768 Leichner, Pierre P.; Janowsky, David S.; Reid, Anne E. Department of Psychiatry, Queen's University, Kingston, Ontario, Canada **Intravenous methylphenidate as a diagnostic and psychotherapeutic instrument in adult psychiatry.** Canadian Psychiatry Association Journal (Ottawa). 21(7):489-496, 1976.

In a study of the diagnostic and psychotherapeutic use of intravenous methylphenidate in adult psychiatry, the reactions of schizophrenics, depressives, alcoholics, and antisocial personalities observed during an interview with a psychotherapist after injection of methylphenidate are described in terms of the following categories: 1) acknowledgement of a "rush" or "high;" 2) ventilation; 3) abreaction; and 4) activation of psychotic symptoms. It was found that an increase in talkativeness and trust during the interviews were the two most common reactions. Activation of preexisting psychotic symptoms was found only in schizophrenics. Neither schizophrenics nor subjects with antisocial personalities acknowledged a "high" or "rush." Alcoholics and antisocial personalities did little abreacting, while depressives showed the most abreaction. It is suggested that the interview serves a psychotherapeutic value in: 1) strengthening the doctor-patient relationship; 2) releasing tension; 3) promoting self-understanding, and 4) demonstrating psychotic and neurotic defenses. It is concluded that, although relatively safe, this technique should only be used in an inpatient setting where appropriate observation can be made through the day after injection. 16 references.

002769 Meyer-Probst, Bernhard; Vehreschild, Torsten. Wilhelm-Pieck-Universitat, Nervenklinik, DDR-25 Rostock 9, Germany **/Controlling concentration disorders in hyperkinetic schoolchildren with Aponeuron./** Zur Beeinflussung der Konzentrationsschwache bei hyperkinetischen Schulkindern mit Aponeuron. Psychiatrie, Neurologie und medizinische Psychologie (Leipzig). 28(8):491-499, 1976.

The therapeutic effects of Aponeuron in controlling hyperkinetic schoolchildren are described. Aponeuron was administered to 38 8- to 13-year-old children of normal intelligence but with poor concentration abilities over a period of 3 to 6 months. Before starting the drug program and after a 3 to 6 month period of continuous medication the children were given a battery of tests, including 6 subtests of HAWIK, the cross-out test, the Kurth test and the Brickenkamp d2 Test. Also, 16 behavior characteristics were evaluated on a 7 step scale by both parents and teachers. The results provide statistical evidence of an increase in concentration power and a decrease in both fatigability and motor restlessness. 14 references.

002770 Nair, N. P. V.; Deutsch, M.; Derkevorkian, K. S.; Udabe, R. Ucha; Ban, T. A.; Lehmann, H. E. Douglas Hospital, Verdun, Quebec, Canada **Doxepin and diazepam in the treatment of hospitalized geriatric patients.** Psychiatric Journal of the University of Ottawa (Ottawa). 1(1-2):35-39, 1976.

A comprehensive clinical study of doxepin and diazepam treatment was conducted in 40 hospitalized geropsychiatric patients. Neither treatment group showed statistically significant improvement on total scores or factors of the Brief Psychiatric Rating Scale (BPRS) or the Nurses' Observation Scale for Inpatient Evaluation (NOSIE). Both groups, however, improved significantly on BPRS items measuring emotional withdrawal, conceptual disorganization, and uncooperativeness. Patients showing clinical improvement showed a significant reduction in the degree of dissociation between the auditory and visual reaction time scores. Two patients on diazepam were dropped from the trial after clinical deterioration, but no doxepin patients were discontinued. Numerous adverse effects occurred in both groups, with drowsiness and dizziness most frequent. Findings suggest that doxepin is better tolerated than diazepam in geriatric patients. (Author abstract modified)

002771 no author. no address **ACTH-4-10 on memory dysfunction.** Convulsive Therapy Bulletin with Tardive Dyskinesia Notes. 1(4):34, 1976.

Results of a study by Small (in press) indicate that ACTH 4-10 administered to patients receiving bilateral ECT had no significant influence on the seizure itself, and unimpressive influence on a variety of memory tasks within the first 47 hours post ECT. Since the testing was done within 47 hours of the ECT, it is not particularly important to patients. What is important is how their memory operates 1 to 2 weeks after ECT. The hope is voiced for an expanded study including patient groups who complain of memory difficulty a few weeks after ECT.

002772 Oettinger, Bernt. Heil-und Pflegestatte fur Epileptiker "Kleinwachau", Kurhaustr. 3, DDR-8107 Liegau-Augustubad, Germany **/Use of psychopharmaceuticals for the treatment of abnormal behavior of oligophrenic epileptics./** Psychopharmaka in der Therapie von Verhaltensauffalligkeiten bei epileptikern. Psychiatrie Neurologie und Medizinische Psychologie (Leipzig). 28(10):635-640, 1976.

Use of psychopharmaceuticals for the treatment of abnormal behavior in oligophrenic epileptics is discussed. Forty one patients were treated with promazine, a phenothiazine derivative, for an average of 266 days. The average daily dose was 200mg. Thirty patients were treated with levomepromazine for an average of 115 days, the daily dose being about 130mg. The two groups of patients were examined for their contactual, impulsive, and affective behavior before, during, and after treatment. The positive results obtained justify the use of the above mentioned psychopharmaceuticals for the therapy of abnormal behavior of oligophrenic epileptics. 17 references. (Journal abstract modified)

002773 Pare, William Paul. University of Delaware, Newark, DE 19711 **The pharmaceutical management of gastric ulceration. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-24264 HC$15.00 MF$8.50 141 p.

Three psychotropic drugs were examined for therapeutic efficacy in preventing development of stomach lesions, or gastric ulcers, in rats. The drugs included the major tranquilizer chlorpromazine, the minor tranquilizer diazepam, and the antidepressant imipramine, the activity/stress ulcer model, which provides a research technique whereby psychophysiological variables can be studied to further study the classic psychosomatic disease, was used. Results suggested that gastric hypersecretion is not a sufficient cause of stomach lesions, and a theory pertaining to the immediate causes of ulcers was presented which suggested that psychosocial stress initiates a hypovolemic condition in the stomach wall plus reduction in gastric motility. The anemic stomach condition renders the mucosa vulnerable to assault and parietal tissue is destroyed.

When psychosocial stress terminates, a parasympathetic rebound occurs with a return of blood to the damaged mucosa, thereby presenting the clinical picture of a hemorrhagic ulcer. It was concluded that the pharmaceutical management of ulcer is best achieved with centrally acting drugs since those that affect local gastrointestinal events leave the relevant CNS processes unmodified. The psychotropic drugs may represent a more useful category of agents because they allow manipulation of CNS/gastrointestinal interactions, allowing the clinician to develop a therapeutic strategy for the disease, which includes psychological as well as physiological events. (Journal abstract modified)

002774 Pires de Oliveira, R. S. Servico de Neurologia e Eletrencefalografia, Sanatorio Antonio Luiz Sayao, Rio de Janeiro, Brazil /**A neurologic, electroencephalographic and psychologic study of FL-121 in patients with cerebral circulatory deficiency.**/ Estudo neurologico, eletrencefalografico e psicologico com FL-121 em pacientes com deficiencia circulatoria cerebral. Revista Brasileira de Medicina (Rio de Janeiro). 33(10):351-359, 1976.

To study the neurological, electroencephalographic, and psychological effects of FL-121 (fludilat) on geriatric patients with cerebrovascular disorders, a double-blind study was carried out. A group of 50 patients, ages 50 to 80 years, diagnosed by encephalogram as having cerebral circulatory deficiency were subjected to a battery of psychological tests derived from the Wechsler Adult Intelligence Scale before and after a course of medication with FL-121. It was found that the medication improved the cerebral electrical activity, augmenting the frequency of base rhythm and bolstering its amplitude. The Wechsler test results also showed considerable beneficial effects from the medication not duplicated by the controls receiving the placebos. Particular improvement was noted in memory in powers of concentration, and in sociability; there was also decreased aggression. 18 references.

002775 Rapoport, Judith L. Unit on Childhood Mental Illness, Adult Psychiatry Branch, NIMH, Bethesda, MD 20014 **Clinical assessment for pediatric psychopharmacology. (Unpublished paper).** Rockville, MD, NIMH, 1976. 23 p.

Diagnostic and clinical assessments used for research in pediatric psychopharmacology are reviewed and discussed. It is suggested that measures of target symptoms, in the context of interaction with setting, and as appropriate to the child's developmental stage, may be more revealing than measurement of syndromal patterns. The criticism is offered that the recent ECDEU Bulletin, which provides a standardized group of behavioral measures for use in pediatric studies, lists primarily behavior rating scales and cognitive tests but fails to mention methods of rating social and emotional functioning. It is stated that evaluations of the child's temperament, educational setting, family functioning, peer relationships, self-report scales, playroom behavior, and possibly projective testing may be used to study drug effects on the child's interpersonal and intrapsychic functioning. Existing studies utilizing these methods are discussed and their validity examined. 55 references.

002776 Rodin, Ernst A.; Rim, Choon Soo; Kitano, Hideki; Lewis, Ronald; Rennick, Phillip M. Department of Neurology and Electroencephalography, Lafayette Clinic, 951 East Lafayette, Detroit, MI 48207 **A comparison of the effectiveness of primidone versus carbamazepine in epileptic outpatients.** Journal of Nervous and Mental Disease. 163(1):41-46, 1976.

A comparison was made of the drug therapy treatment of 45 patients with psychomotor and grand-mal seizures to determine the effectiveness of carbamazepine against primidone added to a therapeutic dose of diphenylhydantoin (DPH). The patients were initially stabilized on therapeutic doses of DPH and one of the test compounds, while all other medications were withdrawn. After 3 months of treatment they were transferred onto the other drug for another 3 month period. Extensive laboratory testing, including anticonvulsant levels, electroencephalograms, and neuropsychological evaluations, was performed. Reports of seizure frequency, side-effects, and laboratory studies every 14 days were made. The results of blind studies of the data indicated that the two drugs did not differ in their effectiveness on seizure control. There were somewhat more side-effects, none serious, with carbamazepine than with primidone. The EEG showed increased fast activity with primidone and increased theta activity with carbamazepine. There was no difference in regard to decrease of electroencephalographic seizure discharges. The patients showed more impairment on a repeatable neuropsychological test battery with primidone than with carbamazepine, and they also showed an increase on the psychopathic deviate scale of the Minnesota Multiphasic Inventory. Depressive feelings, when present, lessened while under treatment with carbamazepine. The results suggest that patients with the seizure types under consideration and unresponsive to DPH alone or to a DPH/phenobarbital combination can be placed on either carbamazepine or primidone while phenobarbital is discontinued. A patient who is intellectually and emotionally intact with no past history of behavioral disturbances may do better on primidone than carbamazepine, because this drug gives fewer side-effects. On the other hand, those patients who have a past history of emotional and/or intellectual disturbances may profit more from carbamazepine. 12 references. (Journal abstract modified)

002777 Rydzynski, Zdzislaw; Siminska, Wieslawa; Grebowicz, Krystyna. Instytut Higieny Psychicznej WAM, ul. Zrodlowa 52, 91-735 Lodz, Poland /**Results of treating nervous tics in children: based on analysis of data of the Psychiatric Clinic of the Military Medical School.**/ Wyniki leczenia tikow u dzieci (na podstawie analizy materialu Kliniki Psychiatrycznej WAM). Psychiatria Polska (Warszawa). 10(5):465-469, 1976.

A study of treating nervous tics is presented based on 15 children (11 boys and 4 girls) treated at the Lodz, Poland, Military Medical School, in whom tics were the only, or major symptom of disease. The children were 6 to 14-years-old, and the average length of hospitalization was 1 month. Although only 1/3 of the children exhibited slight deviation from the norm upon neurological examination, the data gathered from interviews and results of additional tests indicated an organic origin of the tic in nearly all cases. Treatment was based on etiological factors, factors precipitating the onset of the tic, clinical picture, and the somatic state of the patient. Results indicate that in six children, whose clinical symptoms and EEG indicated epileptic disturbances, antiepileptic drugs were successful in therapy, while in six cases positive results were obtained with the use of neuroleptics. In total, 14 different types of treatment were used, ending with complete recovery in 9 cases and significant improvement in 6. 15 references. (Journal abstract modified)

002778 Samec, Von V. Pflegeheim der Stadt Wien-Lainz, Versorgungsheimplatz 1, A-1130 Wien, Austria /**Therapeutic effect of a new hypnotic on sleep disorders in geriatric patients: double-blind trials and long-term study.**/ Die therapeutische

Beeinflussung von Schlafstorungen bei geriatrischen Patienten durch ein neues Hypnotikum: Doppelblindversuche und Langzeitstudie. Wiener Medizinische Wochenschrift (Wien). 126(1-3):23-26, 1976.

Flunitrazepam (Rohypnol: 5-(o-fluorpenyl)-1,3-dihydro-1-methyl-7-nitro-2H-1,4-benzodiazepine-2- ne) was tested as a hypnotic in geriatric patients. The pharmacology of the drug is reviewed. In a double-blind crossover study with placebo, 40 patients, 13 males and 27 females with severe sleep disorders were given 1mg/day flunitrazepam for 1 week. The drug proved superior to placebo in its effect on latency of sleep onset, duration of sleep, depth of sleep, and feelings on awakening. There were no side-effects. In another double-blind crossover study, 2mg/day flunitrazepam was compared with 200mg/day heptabarbital for 3 weeks. Flunitrazepam was found to be superior to both heptabarbital and placebo. Flunitrazepam was next studied in 190 patients at a dosage of 1 to 2mg/day for periods of from 4 months to 6 years. This study showed that morning hangover was less common than with barbiturates and no interference with other medications, physical or psychological dependence, or withdrawal symptoms, were observed. In some patients, the dosage had to be increased from 1mg/to 2mg/day after 4 to 6 weeks. No changes occurred in clinical laboratory tests in any of the patients. 11 references.

002779 Scherrer, P.; Quiniou-Vidalenc. no address **/Remarks on the effects of "Moditen-retard" and Modecate: notes on 65 cases./** Remarques sur l'action du moditen-retard et du modecate: a propos de 65 observations. Annales Medico-Psychologiques (Paris). 2(4):642-656, 1976.

Paper presented at the October 1976 session of the Societe Medico-Psychogique reported the effects of moditen retard on 65 patients. Generally the patients fall into three categories: progressive improvement, relapse, and stationary situation. Modecate was used in cases where Moditen retard was not tolerated or poorly tolerated. The diagnoses were schizophrenia, chronic delirium, and manic-depression. Modecate was better tolerated in some cases, but seemed to be less active than moditen retard. Neither medication had a curing effect, but they considerably diminished psychic disorders even in an advanced stage. They were very effective in hallucination and in stopping the development of delirium. Among side-effects, decrease of sexuality is mentioned. It is recommended that treatment be applied for a sufficently long period to be effective, even though patients or their families may be reluctant. 6 references. (Author abstract modified)

002780 Simpson, Lance L. no address **Drug treatment of mental disorders.** New York, Raven, 1976. 323 p. $13.50.

An overview of drug treatment of mental disorders is presented within the context of the epidemiology, etiology, and course of different psychiatric illnesses. Section 1 deals with the treatment of psychoses. The rationale behind pharmacotherapy is examined, and the short-term and long-term side-effects of pharmacologic agents are comprehensively reviewed. Section 2 covers anxiety and its treatment with particular emphasis on diazepam and chlordiazepoxide therapy. Treatment of affective disorders is considered in Section 3. The final section considers special topics including the use of psychoactive drugs in pediatrics and geriatrics.

002781 Szulczynska, Krystyna. no address **/Some problems of the treatment of bronchial asthma./** Niekotore problemy leczenia dychawicy oskrzelowej. Zdrowie Psychiczne (Warszawa). 17(2):108-117, 1976.

The role of mental and psychosocial factors in the development and course of bronchial asthma is emphasized. Clinical observations show that if antiallergic treatment of bronchial asthma patients is supplemented with rehabilitation of physical efficiency and, as necessary, with tranquilizers combined with psychotherapeutic action on the part of the entire medical staff, this usually leads to improvement. Tranquilizers and neuroleptics used in connection with treatment of bronchial asthma and methods of rehabilitation of physical efficiency are discussed in detail. 27 references. (Journal abstract)

002782 Takahashi, Shinsuke. National Musashi Research Institute of Mental and Nervous Disease, Kodaira-shi, Tokyo, Japan **The action of tricyclics (alone or in combination with methylphenidate) upon several symptoms of narcolepsy.** In: Guilleminault, C., Narcolepsy: proceedings. New York, Spectrum, 1976. 707 p. (p. 625-641).

In a paper given at the First International Symposium on Narcolepsy, Montpellier, France, July 1975, clinical experiences with 68 narcoleptics (and experimental results with 18) were described after treatment with tricyclic antidepressants alone (imipramine, desmethylimipramine, and clomipramine) or in combination with methylphenidate. Effectiveness of drugs was determined from subjective reports by patients, symptom questionnaires designed for narcoleptics, and polygraphic data. Clinically, imipramine controlled cataplexy, hypnagogic hallucinations, and sleep paralysis, but not sleep attacks or daytime sleepiness; methylphenidate in combination seemed slightly effective against sleep attacks or sleepiness. Clomipramine alone or in combination with methylphenidate controlled cataplexy, hypnagogic hallucinations, and sleep paralysis, and decreased sleep attacks. Results showed that the most effective treatment of narcolepsy is clomipramine, followed by imipramine and desmethylimipramine. Some thymoleptic action of tricyclics was also indicated in managing patients' temperament and emotionality. 25 references.

002783 Tennant, Forest S., Jr. Division of Epidemiology, UCLA School of Public Health, UCLA Center for Health Science, Los Angeles, CA 90024 **Outpatient heroin detoxification with acupuncture and staplepuncture.** Western Journal of Medicine. 125(3):191-194, 1976.

Eighteen heroin addicts were treated as outpatients with acupuncture, electrical stimulation and staplepuncture. Results of treatment were compared with results in two similar groups of 18 persons in whom detoxification was carried out using methadone and propoxyphene napsylate. Withdrawal symptoms were relieved for about 2 hours in most of the patients after a treatment episode of acupuncture and electrical stimulation. Staplepuncture, which is manipulation by hand of a surgical staple implanted in the concha of the ear, was reported to relieve withdrawal symptoms at least partially in approximately 40% of subjects. In only one person of the group treated with acupuncture or staplepuncture was complete detoxification achieved, compared with 13 and 10 persons, respectively, in the methadone and propoxyphene napsylate groups. Use of acupuncture and staplepuncture in outpatient clinics may be limited unless techniques can be found that will relieve withdrawal symptoms for a longer period than that observed here. 9 references. (Author abstract)

002784 Tobin, J. M.; Robinson, G. M. Helwig. Northwest Psychiatric Clinic Research Center, Eau Claire, WI **Retrospective evaluation and management of psychiatric patients in older age groups.** Psychiatric Journal of the University of Ottawa (Ottawa). 1(4):145-149, 1976.

To provide information for research and the development of multidisciplinary and interdisciplinary programs for the elderly, the hospital records of 147 patients 60 years of age and older admitted for psychiatric care were analyzed retrospectively. Focus was on the population characteristic, treatment profiles, and the results of haloperidol therapy. An interaction of situational and biological stress and a decline in adaptive coping mechanisms preceded the development of psychiatric symptoms, which occurred twice as many women as men. Functional disorders predominated until about age 70, after which organic brain syndromes occurred more often. About half of the patients had concomitant physical illnesses. More than three fourths of the patients returned to a home setting following hospitalization. Drug treatment was the primary therapeutic approach in 96% of the patients and polypharmacy with agents other than psychotropic compounds increased the need for multidisciplinary and interdisciplinary treatment programs that include psychotherapy, activity therapies, and relationship therapy. Those patients who received haloperidol throughout hospitalization showed significantly more improvement than those in whom haloperidol was used intermittently. 5 references.

002785 Vencovsky, Eugen. Psychiatricka Klinika UK, Plzno, Czechoslovakia **/Therapeutic possibilities of nortriptyline and torecan./** Terapeuticke moznosti podavani nortriptylinu a torecanu. Psychofarmakoterapia Schizofrenii Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 249-252).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, therapeutic possibilities of nortriptyline and torecan are investigated. Nortriptyline, an amitryptyline derivative produced by Lundbeck, was given to 30 patients with nonpsychotic endogenous periodic depressive states, and torecan, a phenothiazine derivative, was given to 20 paranoid and hallucinatory schizophrenics. The study indicates that nortriptyline is a good antidepressant and is almost completely nontoxic, with minimal side-effects. Torecan was found to be an effective antihallucinogenic with some parkinsonian side-effects which can, however, be treated with corrective medication.

002786 Venn, R. D. no address **Electroencephalogram and ergot alkaloids.** Postgraduate Medical Journal (Oxford). 52(Supplement 1):55-56, 1976.

In a paper presented at a symposium on ergot compounds, in London in May 1975, a review of studies was given that showed: 1) with advancing age, the electroencephalogram (EEG) shows increasing slow wave activity and decreasing alpha activity; 2) that some ergot alkaloids affect the EEG; and 3) that clinical improvement in geriatric patients on dihydrogenated alkaloids of ergotoxine correlates with EEG changes. It was concluded that the EEG can be a useful tool in geriatric clinical and pharmacologic research in that it may provide an early indication of: 1) the profile of an investigational new drug; 2) the duration of action; and 3) the optimum dose. It may also provide early guidance of patient selection. 22 references. (Author abstract modified)

002787 Verdeau-Pailles, J. Centre Psychotherapique de Limoux, F-11300 Limoux, France **/Treatment of neuroleptic syndrome with an extended action form of biperiden hydrochloride: 9 month study of 55 hospitalized patients./** Traitement du syndrome neuroleptique par la chlorhydrate de biperidene sous sa forme retard. Etude sur 9 mois de 55 malades hospitalises. Encephale (Paris). 2(4):341-347, 1976.

In a study of the efficacy of extended action biperiden hydrochloride in preventing neuroleptic side-effects 55 females, 20 to over 70 years old, with chronic psychoses were followed for 9 months. Biperiden hydrochloride was very effective in 16 cases, effective in 28, produced little effect in 5, and was ineffective in 3. When biperiden HCl was substituted for another antiparkinsonian already prescribed it had immediate effect in 24 cases, an effect was produced after the 1st month in 4 patients, between the 2nd and 3rd month in 5 patients, and from the 3rd to 9th month in 10 patients. It is concluded that biperiden HCl is sufficiently effective, and if it is well tolerated by the individual it may be expected to produce results after several months of continued prescription. 5 references.

002788 von Hanxleden, Volkhard. Landeskrankenhaus, D-2430 Neustadt/Holstein, Germany **/Long-term treatment of erethismic mental retardation with oxazepam 50./** Zur Langzeitbehandlung des erethischen Schwachsinns mit Adumbran 50. Therapie der Gegenwart (Munchen). 115(11):1942-1944, 1947, 1976.

The use of oxazepam in irritability associated with mental retardation was studied in 30 mentally retarded inpatients ranging from 11 to 60 years of age. The dose of oxazepam was 50mg t.i.d.,and patients were observed for 4 weeks. Improvement was noted in docility with a lessening of aggressivity, motor excitement, and sleep disturbances. Oxazepam was well tolerated and no side-effects were observed. In 20 of 26 patients, dosages of major tranquilizers and antidepressants could be reduced. Oxazepam was then given to 4 male and 5 female patients who had irritability associated with mental retardation. The patients, 23 to 50 years old, received dosages varying from 75 to 200mg/day. Some patients received major tranquilizers concurrently. Oxazepam caused no alteration in blood count, liver function tests, or urinalysis. No patient developed side-effects during the course of the year of treatment. Seven patients had a good or very good response to oxazepam, and the other two had no response. 1 reference.

002789 Von Wild, Klaus; Dolce, Giuliano. Zentrum der Neurologie und Neurochirurgie, Klinikum der J. W. Goeth-Universitat, Schleusenweg 2 -- 16, D-6000 Frankfurt am Main 71, Germany **Pathophysiological aspects concerning the treatment of the Apallic syndrome.** Journal of Neurology (Berlin). 213(2):143-148, 1976.

A test of whether or not the arousal effect elicited by repeated and bilateral stimulation can be produced pharmacologically in man using neuroactivators was undertaken. Results indicate that a pharmacologic activation of cerebral function in Apallic syndrome can be achieved by the IV administration of pyrithioxine (encephabel). The five patients were treated for an increase in vigilance, reactivity, sensory stimulation, and spontaneous motor activity. It is concluded that cortical function might be present even when there is no sign of consciousness and that intensive therapy now makes Apallic syndrome recovery possible, the extent of which depends on the duration of the Apallic syndrome. 20 references.

002790 Von Zerssen, Detlev. Max-Planck-Institut fur Psychiatrie, Munich, Germany **Beta-adrenergic blocking agents in the treatment of psychoses. A report on 17 cases.** In: Carlsson, C., Neuro-psychiatric effects of adrenergic beta-receptor. Munich, Urban & Schwarzenburg, 1976. 120 p. (p. 105-114).

In a paper presented to a symposium on neuropsychiatric effects of adrenergic beta-receptor blocking agents held at

Copenhagen, October 1975, the results of 25 separate therapeutic trials of propranolol and oxprenolol in 17 psychotic patients are reported. Two of the patients were treated with d-propranolol after cessation of dl-propranolol medication. Beta-sympathicolytic treatment led to complete recovery in organic psychoses due definitely in one case and possibly in another case to porphyria; and to moderate or even marked improvement in manic psychoses when the trials could be completed (four cases, one of them treated during two different phases, altogether seven complete therapeutic trials). Treatment was unsuccessful in two manic patients with incomplete trials and in three schizophrenic patients, one of whom received propranolol in doses up to 2800mg per day for 5 weeks. In some of the six patients with schizoaffective psychoses there was a slight to moderate reduction of manic excitement, but no change or even an intensification of paranoid ideas. The observations led to the conclusion that beta-sympathicolytic drugs can be of practical therapeutic value in porphyria psychosis, and that they are of particular theoretical interest because of their apparent antimanic properties. 20 references.

002791 Welling, Else Marie; Zlotnik, Gideon. Bornepsykiatrisk Ambulatorium og Afdeling, Statshospitalet, DK-2600 Glostrup, Denmark **/Treatment of Gilles de la Tourette's syndrome with haloperidol./** Behandling af born med Gilles de la Tourette's syndrom med Haloperidol -- klinisk meddelelse. Nordisk Psykiatrisk Tidsskrift (Kungsbacka). 30(6):421-425, 1976.

Three cases of Gilles de la Tourette's syndrome treated with haloperidol are presented. The anamneses of the cases, three boys between 10 and 11 years old, are described. Haloperidol was given for 52, 12 and 3 weeks respectively and the dosages were initially 0.25mg but increased to 0.5mg every 2 days to finally vary between 1.5mg to 1.75mg per day. The results show a complete disappearence of tic symptoms, except in certain stress situations. 7 references.

002792 Wilson, Charles B.; Gutin, Philip; Boldrey, Edwin B.; Crafts, David; Levin, Victor A.; Enot, K. Jean. Department of Neurological Surgery, University of California School of Medicine, San Francisco, CA 94143 **Single-agent chemotherapy of brain tumors: a five-year review.** Archives of Neurology. 33(11):739-744, 1976.

A brain tumor chemotherapy program established to identify effective single chemotherapeutic agents is reviewed using uniform criteria to allow comparability of results observed with different drugs in 158 patients with intrinsic brain tumors (mostly recurrent malignant astrocytomas). The larger trials with more effective drugs produced these results: carmustine (BCNU) response rate, 47%, with median duration of nine months; lomustine (CCNU), 44% with median duration of six months; procarbazine hydrochloride, 52% with median duration six months; carmustine and vincristine sulfate combined, 44% with median druation of only four months; and BIC (5-3,3-bis (2-chloroethyl)-1-triazeno imidazole-4-carboxamide), 38%, with median duration of five months. Administration of flucocorticoids was not found to bias the frequency of response. Forty seven patients, 26 of whom had responded to the initial drug, received a second drug. Among 26 patients who were evaluable, only four responded to the second drug. 16 references. (Author abstract)

002793 Woggon, B.; Angst, J.; Gmuer, M.; Hess, K.; Hurwitz, E.; Martens, H.; Rothweiler, R.; Steiner, A. Psychiatrische Universitatsklinik Zurich, Forschungsdirektion, Lenggstrasse 31, CH-8029 Zurich, Switzerland /**Clinical double-blind study with two different dosages of maprotiline (150 and 225mg per day).**/ Klinische Doppelblindstudie mit zwei verschiedenen Dosierungen von Maprotilin (150 und 225 mg pro die). Archiv fur Psychiatrie und Nervenkrankheiten (Berlin). 222(1):13-25, 1976.

Maprotiline, in dosages of 150 and 225mg/day, was studied in 20 depressed patients. The 9 males and 11 females had an average age of 48 years. Diagnoses of the patients were schizoaffective psychosis in four, involutional depression in six, endogenous depression in six, reactive depressive psychosis in one, depressive neurosis in two, and cyclothymic personality in one. Ten patients received each dosage, with the high dosage group receiving one 75mg tablet of the drug in the morning and two tablets at night, while the low dosage group received placebo in the morning and two tablets of the active drug at night. Treatment lasted 30 days. Patients were evaluated by the AMP system and the Hamilton Depression Scale on days 0, 2, 5, 10, 15, 20, and 30. There were no differences in improvement between groups using global ratings, neither was there a difference at 30 days between the two groups on the Hamilton Scale. Five patients developed rashes. More fine hand tremor occurred at the high dose. A daily dose of 150mg is recommended for depressed inpatients. 14 references.

002794 Wood, David R.; Reimherr, Frederick W.; Wender, Paul H.; Johnson, Glen E. Department of Psychiatry, University of Utah, College of Medicine, 50 N. Medical Dr., Salt Lake City, UT 84132 **Diagnosis and treatment of minimal brain dysfunction in adults.** Archives of General Psychiatry. 33(12):1453-1460, 1976.

Minimal brain dysfunction (MBD) has long been considered a disorder limited to childhood. A number of longitudinal and adoption studies suggest that MBD may persist into adult life where its existence is concealed by the application of a variety of diagnostic labels. In order to test the hypothesis that MBD does persist into adulthood, 15 putative MBD adults were identified on the basis of current MBD like complaints, self-description of MBD characteristics in childhood, and a parental rating on a standardized form of hyperactivity in childhood. Eleven of the fifteen subjects were given a double-blind trial of methylphenidate hydrochloride, and all 15 were given an open trial of pemoline, imipramine hydrochloride, or amitryptiline hydrochloride. Eight of the eleven showed a significant response to the double-blind trial of methylphenidate. Of the 15, 8 showed a good response to stimulants of tricyclic antidepressants, two showed a moderately favorable response, and five were unresponsive to drug therapy. 44 references. (Journal abstract)

002795 Yevtushenko, S. K. Oblastnaya klinicheskaya bol'nitsa im. Kalinina, Donetsk, USSR /**Combined treatment of Parkinsonism patients with levopa, medantane, and anticholinergic agents.**/ O kombinirovannom lechenii bol'nykh parkinsonizmom preparatami levopa, midantanom i antikholinergicheskimi sredstvami. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova (Moskva). 76(12):1797-1802, 1976.

An experiment was designed to test the effectiveness of levopa combined with medantane, cyclodol, and parkopan in the treatment of parkinsonism. Seventeen of the 42 patients, observed for 6 months to 2 1/2 years, had the atherosclerotic form of the disease and 25 had the postencephalitic form. One group received levopa with either cyclodol or parkopan. The second had levopa with medantane. The third had levopa with medantane and cyclodol. The results show that extended use of levopa with cyclodol is effective in treatment of parkinsonism with hypokinetic and hypertonic syndromes. Levopa

with medantane is effective in treatment of postencephalitic parkinsonism. 30 references.

12 PSYCHOTOMIMETIC EVALUATION STUDIES

002796 Andreoli, A. Centre Psychosocial Universitaire, 16-18, boulevard Saint-Georges, CH-1211 Geneva 4, Switzerland **/Affective-cognitive structures and psychoses: new perspectives of the study of the hallucinatory experience using psychodysleptics./** Structures affectivo-cognitives et psychoses. Nouvelles perspectives de l'etude de l'experience hallucinatoire aux psychodysleptiques. Annales Medico-Psychologiques (Paris). 1(4):501-522, 1976.

Hallucinatory experiences induced by psychotomimetic drugs are discussed and compared with psychoses induced by drug abuse. The neurochemical and neurophysiological bases of the hallucinatory state are discussed, followed by a psychological and psychoanalytic explanation of the hallucinatory state. The affective and cognitive aspects of drug induced hallucinations are stressed. The drugs most discussed are LSD, mescaline, and tetrahydrocannabinol. A multidisciplinary approach provides new information about toxic and endogenous psychoses and about mental development in the child. 121 references.

002797 Bickel, P.; Dittrich, A.; Schoepf, J. Psychiatrische Universitatsklinik, Forschungsdirektion, Postfach 68, CH-8029 Zurich, Switzerland **/An experimental study on the consciousness-altering effect of N,N-dimethyltryptamine (DMT)./** Eine experimentelle Untersuchung zur bewusstseinsverandernden Wirkung von N,N-Dimethyltryptamin (DMT). Pharmakopsychiatrie, Neuro-Psychopharmakologie (Stuttgart). 9(5):220-225, 1976.

The effects of N,N-dimethyltryptamine (DMT) in producing altered states of consciousness was studied in 38 subjects. The 23 males and 13 females, who averaged 31 years in age, were divided into a placebo group of 12 subjects and a DMT group of 26 subjects. The dosage of DMT was 250mcg/kg. Subjects were rated on the von Zerssen Complaint List, the DAE Scale I, and the APZ (Abnormal Psychic State) Questionnaire. Compared with the controls, the DMT subjects showed disturbances of equilibrium, numbness in the hands and feet, heaviness in the legs, dizziness, derealization, euphoria and excitation, visual hallucinations, and changes in visceral experiences. The DMT subjects also showed impairment of memory and attention, changes in body image, depersonalization, anxiety and depression, and delusions. 10 references.

002798 Huszka, Louis; Zabek, D. H.; Doust, J. W. Lovett. Research Laboratory, Queen Street Mental Health Centre, Toronto, Ontario, Canada **Urinary excretion of N,N-dimethylated tryptamines in chronic schizophrenia: a review of the present status of the hypothesis.** Canadian Psychiatric Association Journal (Ottawa). 21(8):541-546, 1976.

The presence of N,N-dimethylated tryptamine (DMT), a hallucinogenic metabolite of serotonin, in the urine of chronic schizophrenics was studied. Urine was collected from seven chronic schizophrenic patients, who were put on a diet containing foods deficient in serotonin. The investigation consisted of seven phases, each lasting 3 weeks: a baseline phase, a phase consisting of phenelzine (MAOI); phenelzine plus a placebo; phenelzine plus glycine; another phase with phenelzine; and a last baseline phase. Two patients were not given psychoactive drugs as a control variable, while other patients continued taking medication prescribed. It is suggested that the existence of toxic methylated tryptamines is not as common as it might be if the methylation hypothesis of schizophrenia had wide acceptance. The occurrence of any postulated tertiary amines seems to grow rarer the more specific the methods used to search for them. It is concluded that DMT is a psychedelic drug but that there is no evidence that it acts in this way other than when administered to the subject. 43 references. (Author abstract modified)

13 MECHANISM OF ACTION: PHYSIOLOGICAL, BIOCHEMICAL AND PHARMACOLOGICAL

002799 Adams, T. no address **Trial of antidepressants.** New Zealand Medical Journal (Dunedin). 565(83):415, 1976.

A double-blind trial comparing the relative efficacy of two tricyclic antidepressants is discussed. The respondent takes issue with the statement that the patient sample, which included patients reporting feelings of despair and hopelessness and depressed ideation, excluded potentially suicidal patients. It is suggested that the sample consisted of the group type that yields the greatest number of suicides.

002800 Biederman, Joseph; Rimon, Ranan; Ebstein, Richard; Zohar, Joseph; Belmaker, Robert. Jerusalem Mental Health Center, Ezrath Nashim, Jerusalem, Israel **Neuroleptics reduce spinal fluid cyclic AMP in schizophrenic patients.** Neuropsychobiology (Basel). 2(5/6):324-327, 1976.

Cerebrospinal fluid (CSF) cyclic AMP was measured in schizophrenic patients to test the theory that neuroleptics are clinically effective in schizophrenia as a result of their inhibitory action on dopamine transmission. Cyclic AMP in the CSF was determined in a group of 10 schizophrenic patients before neuroleptic drug treatment and after a mean of eight weeks' antipsychotic drug therapy. For eight patients with marked to moderate treatment response a significant decline in CSF cyclic AMP was observed. This result is consistent with the theory that blockade of postsynaptic dopamine receptors is a major mechanism of the antipsychotic action of neuroleptic drugs. 16 references. (Author abstract modified)

002801 Bockenheimer, S.; Lucius, G. Psychiatrische und Nervenklinik der Universitat Freiburg, Hauptstrasse 5, D-7800 Freiburg/Br., Germany **/Therapy with dimethylaminoethanol (Deanol) in neuroleptic-induced extrapyramidal hyperkinesia./** Zur Therapie mit Dimethylaminoathanol (Deanol) bei neuroleptikainduzierten extrapyramidalen Hyperkinesen. Archiv fur Psychiatrie und Nervenkrankheiten (Berlin). 222(1):69-75, 1976.

The effect of Deanol (dimethylaminoethanol), a direct precursor of intracerebral acetylcholine, was studied in 20 chronic, hospitalized psychiatric patients who had oral tardive dyskinesia and (in 15 cases) tardive dyskinesia of the extremities, in order to test the hypothesis that a CNS relative lack of acetylcholine is the underlying mechanism in tardive dyskinesia. The 5 men and 15 women ranged in age from 28 to 75 years, with an average age of 55 years. The diagnosis was schizophrenia in 18, cyclothymia in one, and cerebral sclerosis in one. The average length of drug therapy was 12 years, with most of the patients receiving chlorperphenazine and levomepromazine. The trial of Deanol followed a double-blind, crossover protocol, with placebo and drug periods lasting 5 weeks each, and a 3 day washout period between trials. The initial dose of Deanol was 300mg/day, and it was increased according to a fixed schedule until a maximum of 1500mg/day was reached the 5th week. Deanol was effective in only some of the patients, and then only in the oral dyskinesia. 21 references.

002802 Bolton, Ralph. Pomona College, Claremont, CA **Andean coca chewing: a metabolic perspective.** American Anthropologist. 78(3):630-634, 1976.

Metabolic factors involved in the etiology of Andean coca chewing are presented. Previous studies suggesting psychological/psychedelic factors for coca chewing are reviewed. While coca may have euphoria producing properties, Andean Indians do not consume large enough quantities to produce such effects. Reasons the Indians give for coca chewing are: energy and relief of fatigue, warmth, and relief of hunger. Research into nutritional and metabolic aspects of coca use are briefly reviewed. Analysis of data on coca use indicates that moderate hypoglycemics and individuals living at high altitudes and with restricted protein intakes tend to consume greater quantities of coca. It is suggested that this may indicate that coca has fundamental metabolic functions for large numbers of Indians with glucose homeostasis difficulties. The uses of coca in Andean Indian culture are complex and include ritual, exchange and social interaction. It is concluded that mounting evidence for the metabolic functions of coca in the Indian diet suggests that efforts to abolish coca use may be misguided. 19 references.

002803 Chase, Thomas N. Laboratory of Neuropharmacology, National Institute of Neurological and Communicative Disorders and Stroke, NIH, Bethesda, MD 20014 **Rational approaches to the pharmacotherapy of chorea.** In: Yahr, M., The basal ganglia. Vol. 55. New York, Raven Press, 1976. 474 p. (p. 337-350).

In a paper presented at the 55th meeting of the Association for Research in Nervous and Mental Disease, theoretical approaches to the pharmacological symptomatic relief of Huntington's disease (HD) were explored and relevant experiment results were reviewed, emphasizing limitations caused by lack of detailed information on the synaptic connections made and transmitters used by neural systems within the basal ganglia, especially those characteristically involved in this disorder. Hope for the rational development of improved pharmacologic treatments for HD arises largely from the success of l-DOPA therapy in Parkinsonism. The ability of such therapy to improve Parkinsonian signs may be contingent on unusual circumstances not found in other degenerative brain disorders, however, and studies are ongoing to identify potential candidates for the striatal neurohumoral system whose modification might benefit HD. These studies have concentrated on the dopaminergic, noradrenergic, serotonergic, and cholinergic systems, as well as the gamma-aminobutyric acid (GABA) system. Results suggest that either GABA or acetylcholine containing neurons, or both, may be involved in HD pathogenesis. Cells of both types may serve as interneurons within the striatum. GABA-ergic neurons also comprise part of the striatal efferent system. The development of pharmacologic techniques to selectively modify these systems thus assumes critical importance for testing the concept of neurohumoral replacement in non-Parkinsonian states, as well as for improving ability to treat HD patients. 85 references.

002804 Costa, Jonathan L.; Murphy, Dennis L. Laboratory of Clinical Science, NIMH, 9000 Rockville Pike, Bethesda, MD 20014 **Alterations in human-platelet serotonin uptake following the addition of thrombin and A23187. (Unpublished paper).** Bethesda, MD, NIMH, 1976. 7 p.

In order to measure the effect of both thrombin and the ionophore A23187 on the uptake of labeled serotonin (5-HT) across the platelet plasma membrane, human platelet rich plasma was prepared and platelet endogenous 5-HT was labeled. Release of 3H-5-HT was measured 30 seconds after the addition of the releasing agent and percent release was calculated as the percent of label lost in comparison with that found in platelets fixed with formaldehyde prior to the addition of human thrombin or A23187. Uptake during the 30 second release period was essentially normal when doses causing no 5-HT release were added. Higher doses of thrombin produced increasing amounts of release and a proportionate reduction in uptake. Similar dose related effects were found with A23187. Uptake for a 2 minute period measured up to 60 minutes following thrombin or thrombin and hirudin addition were markedly reduced compared to control values. Data suggest that, in addition to inducing vesicle release, treatment with thrombin or A23187 alters the plasma membrane uptake of 5-HT and delineate a significant advantage in the use of thrombin for studies of 5-HT uptake. 4 references.

002805 Dixon, Ross; Brooks, Marvin A.; Postma, Edward; Hackman, Martin R.; Spector, Sidney; Moore, James D.; Schwartz, Morton A. Dept. of Biochemistry and Drug Metabolism, Hoffmann-La Roche Inc., Research Division, Nutley, NJ 07110 **N-desmethyldiazepam: a new metabolite of chlordiazepoxide in man.** Clinical Pharmacology and Therapeutics. 20(4):450-457, 1976.

The identification and determination by gas chromatography, mass spectrometry, and radioimmunoassay of N-desmethyldiazepam (a known metabolite of diazepam) in the plasma of human subjects receiving chlordiazepoxide is described. In subjects receiving a single 30mg oral or intravenous dose of chlordiazepoxide, measurable levels of N-desmethyldiazepam in plasma (10 to 60ng/ml) were obtained 24 hr to 72 hr after administration. In 5 subjects receiving 10mg of chlordiazepoxide three times a day, steady state levels of N-desmethyldiazepam in plasma were reached after about 1 wk of administration. The mean maximum and minimum steady state levels of N-desmethyldiazepam were 260ng/ml and 220ng/ml of plasma, respectively. Similar steady-state levels were observed on treatment with 30mg of chlordiazepoxide over 24 hr. 20 references. (Author abstract modified)

002806 Endler, Siegfried; Muller, Eckhart. Nervenklinik der Medizinischen Akademie, Nordhauserstr. 74, DR-50 Erfurt, Germany **/Contribution to the management of focal EEG changes with intravenous administration of diazepam (Faustan)./** Ein Beitrag zur Beeinflussung von EEG-Herdstorungen unter intravenoser Diazepamgabe (Faustan). Psychiatrie, Neurologie und Medizinische Psychologie (Leipzig). 28(4):229-235, 1976.

Management of focal EEG changes with intravenous administration of diazepam (Faustan) in 34 patients, including 20 females and 14 males 18 to 69 years old, with focal EEG modifications, is described. Brain tumor was verified in all cases. EEG analysis showed bioelectric functional disturbances may remain unchanged, may be provoked or abolished; apparently etiological aspects are not decisive. According to the results, the value of this provocation method for the differentiation of space occupying intracranial processes and cerbrovascular disturbances should be regarded with caution. 10 references. (Journal abstract modified)

002807 Engel, Jorgen. Department of Pharmacology, University of Gothenburg, Sweden **The mode of action of psychotropic drugs.** In: Advances in the drug therapy of mental illness. Geneva, World Health Organization, 1976. 168 p. (p. 51-60).

Experiments on the action modes of antipsychotic drugs and several drugs known to cause drug dependence are discussed.

It is postulated that many drugs that influence human mental functions and behavior in man and animals act by interfering with monoamine neurotransmission in the brain. Three groups of drugs are discussed: 1) antipsychotic drugs such as phenothiazine, butyrophenone groups, chlorpromazine and haloperidol; 2) lithium salts; and 3) amphetamine and ethanol. The finding that pretreatment with a specific inhibitor of the tyrosine hydroxylase prevents the stimulant and euphoriant action of ethanol indicates that the central catecholamines may be involved in the mediation of the ethanol induced stimulation and euphoria in man. Results support the hypothesis that a relationship exists between the euphoriant action of drugs causing drug dependence and their effects on central catecholamine mechanisms. 25 references.

002808 Evans, J. M.; Hogg, M. I. J.; Rosen, M. Department of Anaesthetics, University Hospital of Wales, Cardiff CF4 4XW, Wales **Reversal of narcotic depression in the neonate by naloxone.** British Medical Journal (London). No. 6044:1098-1100, 1976.

The effects of naloxone on narcotic ventilatory depression in the neonatal infant were investigated. Naloxone, 40mg, was administered intravenously one minute after birth to 20 out of 44 neonates whose mothers had been given pethidine in labor. These neonates were compared with 20 others whose mothers had had only lumbar epidural block. Alveolar PCO2, alveolar ventilation, and ventilatory rate were measured 10 and 30 minutes after birth. The untreated neonates of mothers who had pethidine showed significant ventilatory depression compared with infants in the epidural and naloxone treated groups. The naloxone treated neonates were comparable with the epidural group, although the effects of naloxone were diminishing at 30 minutes. It is concluded that naloxone is an effective narcotic antagonist which should be considered to be the drug of choice for treating narcotic depression in the neonate. 5 references. (Author abstract)

002809 Farkas, Tibor; Dunner, David L.; Fieve, Ronald R. New York State Psychiatric Institute, New York, NY **L-tryptophan in depression.** Biological Psychiatry. 11(3):295-302, 1976.

Clinical data are presented regarding the antidepressant effect of L-tryptophan, the amino acid precursor of serotonin. L-tryptophan was administered to 16 patients diagnosed for primary affective disorder in a double-blind study of its potential antidepressant efficacy. Antidepressant responses were observed in one of 10 unipolar patients and in three of six bipolar patients. The results confirm previous findings that the antidepressant response is absent in unipolar patients and suggest that further clinical trials of L-tryptophan in bipolar patients are indicated. The results are further discussed in the context of possible interactions of amines with electrolyte systems in the etiology of affective illness. 27 references. (Author abstract modified)

002810 Frausto da Silva, J. J. R.; Williams, R. J. P. Centro de Quimica Estrutural, Instituto Superior Tecnic, Lisbon, Portugal **Possible mechanism for biological action of lithium.** Nature (London). 263(5574):237-239, 1976.

A possible mechanism of action for lithium as a therapeutic drug is offered, and it is suggested that the active agent is undoubtedly the lithium cation. The dose level, around 1 mM, in the body, is extremely high and the most likely action of lithium is that it challenges one of the common biological cations Na+, K+, Mg2+ and Ca2+. Chemical affinities measured by absolute values of stoichiometric stability constants do not give the true tendency for preferential binding of a certain metal ion if other potential complexing agents are also present. The free metal ion content of the compartment under discussion must be known. It is concluded that a better approach is to use 'conditional' stability constants, which are constants valid for the medium in which the reaction is taking place. 12 references. (Author abstract modified)

002811 Garattini, S. Mario Negri Institute of Pharmacological Research, Milan, Italy **Variability of Psychotropic drug response: the contribution of biochemical pharmacology to its elucidation.** In: Advances in the drug therapy of mental illness. Geneva, World Health Organization, 1976. 168 p. (p. 61-68).

The variability of psychotropic drug response is examined in terms of improved treatment of mental diseases and tailored drug administration to individual needs. A survey of the factors responsible for variability in the effects of drugs permits identification of two main groups: 1) different capacities of the individual to distribute and metabolize psychotropic drugs; and 2) different effects of psychotropic drugs in relation to the variability of the organic substrates on which they interact. It is concluded that the examples discussed indicate the complexity of the action of psychotropic drugs. 43 references.

002812 Goodwin, F. K.; Post, R. M.; Jimerson, D. Intramural Research Program, NIMH, Bethesda, MD 20014 **Studies of CSF amine metabolites in affective illness and in schizophrenia.** In: Airaksinen, M., CNS and behavioural pharmacology. Elmsford, New York, Pergamon Press, 1976. 344 p. v. 3. (p. 285-297).

In a paper presented at the Sixth International Congress of Pharmacology held in Helsinki, Finland in July, 1975, studies of the levels of amine metabolites in the cerebrospinal fluid (CSF) of patients with affective illness and schizophrenia are reviewed with emphasis on the effects of various pharmacological treatments on these metabolites and the relationship of the data to the amine hypotheses of affective illness and the amine hypotheses of schizophrenia. The potential benefits and limitations of such studies and the validity of the probenecid technique in the estimation of CNS amine turnover are discussed. The study results are compared with those of other researchers and possible reasons for the discrepancies in the results are suggested. Amine metabolite studies in affective illness have revealed striking biochemical variability within a group of depressed patients who are apparently relatively homogenous clinically, suggesting that biologically identifiable subgroups of patients may exist. Subdivision of depressed patients according to subsequent response to drug treatment has revealed that: 1) responders to tricyclic antidepressants had higher pretreatment accumulations after probenecid of 5-hydroxyindoleacetic acid (5-HIAA) and homovanillic acid (HVA) than nonresponders; 2) nonresponders to lithium treatment had lower HVA accumulations than did responders; and 3) 3-methoxy-4-hydroxyphenyglycol (MHPG) is not predictive of differential response to these drugs. It has also been round that widely diverse treatments effective in depressions (tricyclic antidepressants, lithium, monoamine oxidase inhibitors, and electroconvulsive therapy, but not neuroleptics) all produce an eventual decrease in 5-HIAA accumulation in the CSF. The most consistent finding in studies of CSF amine metabolites in schizophrenia is an alteration in the dopamine (DA) metabolite homovanillic acid (HVA). In addition, the major pharmacological treatments effective in schizophrenia (the neuroleptics) have a relatively selective effect on HVA in the CSF. It is posited that the CSF metabolite data do not support a single amine model of affective illness or the

hypotheses that depression is related to a functional deficit of serotonin (5ehydroxytryptamine), norepinephrine, or DA while mania is associated with an excess of these amines and the data are only partially consistent with the DA hypotheses of schizophrenia. 55 references.

002813 Gram, Lars F.; Andreasen, Per Buch; Overo, Kerstin Fredricson; Christiansen, Johannes. Department of Pharmacology, University of Copenhagen, 20, Juliane Maries Vej, DK-2100 Copenhagen O, Denmark **Comparison of single dose kinetics of imipramine, nortriptyline and antipyrine in man.** Psychopharmacology (Berlin). 50(1):21-27, 1976.

The single dose kinetics of imipramine (IP), nortriptyline (NT), and antipyrine (AP) were compared in seven healthy subjects. Test doses of AP were given intravenously, and test doses of IP and NT were given both orally and by intravenous infusion. Compared to NT, IP had statistically significant higher clearances, shorter half-lives, and smaller apparent volumes of distribution. There was a significant correlation between apparent volume of distribution of IP and NT but only a weak correlation between the clearance measurements of the two compounds. Systemic clearance of AP and IP showed some positive correlation, whereas there were no significant correlations between AP and NT kinetics. The data indicate that interindividual and intraindividual variations in hepatic blood flow may influence the measurements. Other possible sources of variability are individual differences in hepatic extraction kinetics and differences in binding to blood constituents. 41 references. (Author abstract modified)

002814 Gray, J. A. Department of Experimental Psychology, Oxford University, Oxford, England **The neuropsychology of anxiety.** In: Sarason, I., Stress and anxiety. Washington, Hemisphere, 1976. 365 p. v.3. (p. 3-26).

In this chapter in a volume on stress and anxiety, the neuropsychology of anxiety is discussed. Research with antianxiety drugs is reviewed and support the hypothesis that anxiety is a central state that mediates behavioral responses to stimuli that signal either punishment or nonreward. The principal site of action of the antianxiety drugs is the dorsal ascending noradrenergic bundle, originating in the locus coeruleus in the brainstem and innervating the hippocampus, the septal area, and the neocortex. This pathway modulates septal control of hippocampal electrical activity, and this modulating influence is altered by the antianxiety drugs. 65 references.

002815 Greenacre, J. K.; Petrie, A.; Coxon, A.; Reid, J. L. Dept. of Clinical Pharmacology and Medicine, Royal Postgraduate Medical School, Hammersmith Hospital, London W12, England **Comparison of levodopa with carbidopa or benserazide in Parkinsonism.** Lancet (London). No. 7982:381-384, 1976.

The therapeutic efficacy and side-effects of two preparations of levodopa with extracerebral decarboxylase inhibitors was compared in 19 patients with idiopathic Parkinsonism in a blind randomized crossover trial. The mean daily dose of levodopa was 658 plus or minus 64mg/day when given together with carbidopa 66mg/day and 605 plus or minus 59mg/day when levodopa was combined with benserazide 151mg/day. There was no significant difference between the treatment regimens either in beneficial effects on Parkinsonian symptoms and signs or in the adverse effects of levodopa assessed by a clinical observer unaware of the treatment given. Of the 19 patients studied, 9 preferred the carbidopa preparation, 8 preferred the benserazide preparation, and 2 had no preference. It is concluded that there is no significant difference in therapeutic effects or adverse reactions between the two commercially available decarboxylase inhibitor containing preparations. Central nervous system actions and side-effects depend on the daily dose of levodopa, regardless of the different ratios of decarboxylase inhibitors to levodopa. 15 references. (Author abstract)

002816 Haik, Z.; Karplus, M.; Gorodischer, R. Soroka Medical Center, Beersheba, Israel **Caffeine in the prevention of apnea of prematurity.** Israel Journal of Medical Sciences (Jerusalem). 12(12):1515-1516, 1976.

A paper given at the 35th meeting of the Israel Physiological and Pharmacological Society on caffeine in the prevention of apnea of prematurity is summarized. Caffeine was administered to 5 premature infants, 24 to 33 weeks, suffering from severe apneic episodes, accompanied by bradycardia, elevated CO2 pressures and low pH and oxygen pressure. Whenever tachycardia appeared, the dose was reduced. No other toxic effects were clearly identified. Apneic episodes were abolished in four infants and markedly reduced in one. Discontinuation of the caffeine was followed by apneic episodes at variable times. Readministration was reported again to abolish or markedly reduce the apneic episodes and cause a return of arterial blood gases to normal values.

002817 Hall, R. A.; Griffin, R. B.; Moyer, D. L.; Hopkins, K. H.; Rappaport, M. Institute for Medical Research of Santa Clara County, 751 South Bascom Avenue, San Jose, CA 95128 **Evoked potential, stimulus intensity, and drug treatment in hyperkinesis.** Psychophysiology. 13(5):405-418, 1976.

The responses of 45 hyperkinetic (HK) boys to light flashes of four different intensities were measured with averaged visual evoked potential (AVEP). Latency, amplitude and stability data, including the slope of the regression of these measures with flash intensity, were obtained in initial and replicate samples of HK and control subjects. The data failed to support the hypotheses that HK children show small response to weak stimuli and normal to increased response to strong stimuli or "hyperaugmentation," that they show increased response to weak stimuli or "reduction" when they are treated with dextroamphetamine, and that behavioral responsiveness to this drug is related to the degree of augmentation. The data also fail to support the hypothesis that detection of AVEP abnormalities in HK subjects is enhanced by testing in an attending condition. 17 references. (Author abstract modified)

002818 Herrschaft, H. Neurologische Klinik, Ostmersheimer Strasse 200, D-5000 Koln-Merheim, Germany /**Cerebral hemodynamics and brain metabolism: measurement procedures, physiology, pathophysiology, modifications in organic brain disease, pharmacology.**/ Gehirndurchblutung und Gehirnstoffwechsel. (Messverfahren, Physiologie, Pathophysiologie, Veranderungen bei den hirnorganischen Erkrankungen, Pharmakologie). Fortschritte der Neurologie, Psychiatrie etc. (Stuttgart). 44(5):195-319, 1976.

A comprehensive review summarizes recent development (mostly from 1960 to 1975) in research on cerebral hemodynamics, metabolism and induced cerebral phenonema. Measuring techniques, physiology, pathology, alterations resulting from diseases, and the effects of pharmacological substances, narcotics, and x-rays on the brain are discussed. Effects of the following types of drugs are presented: sympathomimetic substances, beta receptor stimulators and beta blockers, alpha-receptor blockers, antiadrenergic substances, histamines, serotonin, ganglion blockers, adenosine derivatives, inorganic ions, and vasoactive substances. 1106 references.

002819 Klee, Werner A. NIMH, Laboratory of General and Comparative Biochemistry, Bethesda, MD 20014 **Endogenous opiate peptides. (Unpublished paper).** Bethesda, MD, NIMH, 1976. 43 p.

The conceptualization, isolation and characterization, and present knowledge of endogenous opiate peptides are presented. Pharmacological evidence for and biological studies of the opiate receptor are reviewed, and the hypothesized coupling action with adenylate cyclase is explained. The role of adenylate cyclase in the mechanism of addiction is discussed, and various endogenous opiates are reviewed. The enkephalins are characterized as endogenous opiate pentapeptides of defined structure, and the structural relationship between the enkephalins and morphine is described. The physiological role of the endogenous opiate peptides is discussed. 73 references.

002820 Koyama, Tsukasa; Aikawa, Hishishi; Haraoka, Yoichi; Manabe, Ryokichi; Ito, Naoki; Tsukamoto, Ryuzo; Saito, Yoshiro; Asano, Yu; Satomi, Ryuta. Department of Neuropsychiatry, Asahigawa Municipal Hospital, Asahigawa, Hokkaido, Japan **Clinical research into amine metabolism products in the spinal fluid (II) -- three cases of consciousness impairment that showed improvement after L-dopa administration -- liver-related brain disease and dopamine and serotonin metabolism.** Psychiatria et Neurologia Japonica (Tokyo). 78(8):578-579, 1976.

In a paper presented at the 48th Hokkaido Psychoneurological Symposium held in December 1975 at Sapporo, Japan, the effects of L-dopa administration in three cases of liver related brain disease were described. Dosage of 300 to 500mg of L-DOPA was administered intravenously and definite clinical results were noted: brainwaves returned to normal and ammonia values in the blood serum returned to normal. In two other cases, ammonia values remained above average and psychotic symptoms persisted. Causal factors in liver related brain disease were found to be complicated, and the effects of L-DOPA were thought to be supplemental effects on catecholamine metabolism.

002821 Langer, Gerhard; Heinze, Gerhard; Reim, Beatrix; Matussek, Norbert. Albert Einstein College of Medicine, Bronx, NY 10461 **Reduced growth hormone responses to amphetamine in "endogenous" depressive patients: studies in normal, "reactive" and "endogenous" depressive, schizophrenic, and chronic alcoholic subjects.** Archives of General Psychiatry. 33)12):1471-1475, 1976.

In view of the fact that several pharmacological stimulation tests of the pituitary/hypothalamic system have been used to investigate psychiatric disorders, amphetamine sulfate was used as a stimulus for human growth hormone (HGH) release in various psychiatric patients. Peak HGH release after a single intravenous administration of amphetamine sulfate was significantly lower in nine endogenous depressives and significantly higher in seven reactive depressives as compared to normal subjects, whereas peak HGH release in eight schizophrenics and six chronic alcoholics did not differ significantly from that in normal subjects. Considering the pharmacological properties of amphetamine and the present concepts of neural regulation of HGH, findings are compatible with a current hypothesis that altered brain monoaminergic activities represent one biological correlate of depressive disorders. 49 references. (Journal abstract)

002822 Latham, A. N.; Turner, P.; Franklin, C.; Maclay, W. McMaster University Medical Center, Hamilton, Ontario L8S 4J9, Canada **Phenobarbitone-induced urinary excretions of D-glucaric acid and 6beta-hydroxycortisol in man.** Canadian Journal of Physiology and Pharmacology (Ottawa). 54(5):778-782, 1976.

The urinary excretions of D-glucaric acid and 6beta-hydroxycortisol were determined in normal subjects before, during, and after 14 days treatment with placebo or phenobarbitone. The excretion of both metabolites was significantly potentiated by phenobarbitone and returned to baseline values 1 month after treatment was withdrawn. It is suggested that the determination of urinary D-glucaric acid reflects the activity of the hepatic microsomal mixed function oxidase system after the administration of an inducing agent such as phenobarbitone. 11 references. (Author abstract)

002823 Lavene, D.; Longchampt, J.; Guillaume, M. F.; Kiger, J. L. Pharmacokinetic Research Center, Sandoz Ltd., Rueil-Malmaison, France **Drug interactions of the components of Optalidon after oral administration.** International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 13(4):235-245, 1976.

An investigation involving seven successive studies was undertaken on several groups of 10 to 14 volunteers, in order to evaluate any drug interaction between the three active components of Optalidon, namely amidopyrine (A), butalbital (B), and caffeine (C). Each component was investigated after oral administration, alone and in combination either with one of the others (i.e. A+B, B+C, C+A) or with both of the others in Optalidon (A+B+C). The plasma concentration and urinary excretion antipyrine and acetamino-4-antipyrine, were also measured in the urine. Based on a pharmacokinetic model, the following conclusions can be drawn: a) there is no change in bioavailability due to the combination of the three components in Optalidon in respect to their single administration, b) concerning the absorption half-life, there is no change for amidopyrine. Only caffeine and butalbital show a statistically significant interaction in respect to this parameter and, as a consequence, differences in the time and value of the maximal plasma concentration in Optalidon. However, these differences are scarcely of any clinical relevance. 9 references. (Author abstract modified)

002824 Malmgren, Harry; Heykants, Jos. AB LEO, Helsingborg, Sweden **On the clinical pharmacology of penfluridol.** Nordisk Psykiatrisk Tidsskrift (Kungsbacka). 30(5):392-399, 1976.

Pharmacokinetic experiments in penfluridol maintenance with seven schizophrenic inpatients, aged 22 to 56 years, maintained on a regular single weekly dose varying between 20 to 80mg are presented. The amount of penfluridol from plasma samples was determined by gas liquid chromatography. Concentrations of penfluridol in urine and in feces were also determined. The maximum plasma concentrations were reached 4 to 8 hours after administration and there was a good correlation between the steady state plasma concentration and the dosage, expressed as mg/kg bodyweight. Most of the unchanged penfluridol was excreted in the feces and only traces of nonmetabolized substance were found, in conjugated form, in the urine. The mean absorption of penfluridol was estimated to be 70%. Patients treated with weekly doses up to 80mg showed no signs of accumulation of the drug during the nine week observation period. 12 references.

002825 Mendlewicz, J. no address **/Lithium salts in psychiatry: importance of genetic factors./** Les sels de lithium en psychiatrie: Importance des facteurs genetiques. Concours Medical. No.7(Supplement):8-11, 1976.

The relationship of genetic factors to the effectiveness of lithium therapy is discussed. Genetic factors influence the metabolism of certain drugs and are involved in the etiology of the major psychoses. Through a study of the effect of monoamine oxidase inhibitors and tricyclic drugs, it may be inferred that there are two different genetic subgroups of depression: some manic-depressives respond well to lithium and others do not. It may be that the good responders metabolize lithium more slowly than do the poor responders. Lithium has a better prophylactic action in bipolar forms of depression and also in parents of bipolar patients. The genetic hypothesis was confirmed by a study in bipolar monozygotic twins. Modifications of neuromediators appear to be of secondary importance; membrane differences at the peripheral cellular level have been studied and they appear to be tied to genetic factors. 22 references.

002826 Muhlau, Gerhard; Reichel, Gerhard; Stahl, Joachim; Both, Reinhard. Klinik fur Neurologie und Psychiatrie hans Berger, Friedrich-Schiller-Universitat, Philosophenweg 3, DDR-69 Jena, Germany **/Determination of variation in the speed of conduction of motor fibers and of the diphenylhydantoin (phenytoin) and diazepam (Faustan) effect on it./** Die Bestimmung der Streubreite der Leitgeschwindigkeit motorischer Fasern und ihre Beeinflussung durch Diphenylhydantoin (Phenytoin) und Diazepam (Faustan). Psychiatrie, Neurologie und Medizinische Psychologie (Leipzig). 28(7):423-429, 1976.

The effect of diazepam and diphenylhydantoin on conduction in the right ulnar nerve was studied in 20 patients ranging in age from 15 to 52 years old. Ten patients received 300mg/day diphenylhydantoin and ten received 15mg/day diazepam for 10 days. A double stimulus method was used to measure conduction in the motor fibers. Both diazepam and diphenylhydantoin significantly decreased maximal and minimal rates of conduction. 20 references.

002827 Nadler, E.; Korczyn, A. D.; Gitter, S. Sackler School of Medicine, Tel Aviv, Israel **Hemolytic and antihemolytic effects of antipsychotic drugs.** Israel Journal of Medical Sciences (Jerusalem). 12(12):1527, 1976.

A summary of a paper delivered at the 36th meeting of the Israel Physiological and Pharmacological Society on hemolytic and antihemolytic effects of antipsychotic drugs is presented. It was found that the rate of hemolysis depended on the concentration of the drug. This was in contrast to the antihemolytic effect which occured immediately following exposure to the drug. It is concluded that the hemolytic effect of chlorpromazine is caused by an action of the drug on sites which are relatively inaccessible to the drug. By exposing red blood cells to chlorpromazine in hypotonic media, the swelling of the cells and the stretching of the membranes allow chlorpromazine easier access to the hemolytic sites.

002828 Perrin, J. H.; Hulshoff, A. Farmaceutisch Laboratorium, Rijksuniversiteit Utrecht, Catharijnesingel 60, Utrecht, The Netherlands **The binding of phenothiazines and related compounds to human serum albumin.** Journal of Pharmacy and Pharmacology (London). 28(10):793-794, 1976.

In a letter to the editor, an experiment is described in which Rm values (binding constants and charge transfer complexation constants) of a series of phenothiazines on human serum were measured to reexamine the hypothesis that binding phenomenon is the result of predominantly electronic rather than hydrophobic interactions. Rm was measured using oleyl alcohol, and aqueous methanol with Kieselguhr as a support phase. In contrast to previously reported results, it is suggested that hydrophobic rather than electronic interactions are responsible for binding. 15 references.

002829 Poust, Rolland I.; Mallinger, Alan G.; Mallinger, Joan; Himmelhoch, Jonathan M.; Neil, John F.; Hanin, Israel. Department of Pharmaceutics, University of Pittsburgh, Pittsburgh, PA 15261 **Effect of chlorothiazide on the pharmacokinetics of lithium in plasma and erythrocytes.** Psychopharmacology Communications. 2(3):273-284, 1976.

The effect of chlorothiazide on the pharmacokinetics of lithium in both plasma and erythrocytes (RBC) was studied in normal adult males. This was accomplished by administering single doses of lithium carbonate alone and concurrently with chlorothiazide. Thiazide administration resulted in increases in plasma and RBC concentrations of 26.2% and 25.4%, respectively, as well as a 26.5% decrease in renal lithium clearance. The data were analyzed in terms of a two compartment pharmacokinetic model as previously reported. The results of this analysis showed that the change in renal lithium clearance could be accounted for by a 24.1% reduction in the value of ke, the excretion rate constant. It was also shown that changes in plasma lithium concentration during chronic lithium therapy would be expected to increase by 25% to 30% when chlorothiazide therapy is employed. The model also predicts that changes in RBC concentrations would parallel those occurring in plasma and thus no change in the RBC/plasma lithium ratio would be expected. 26 references. (Author abstract)

002830 Prichep, Leslie S.; Sutton, Samuel; Hakerem, Gad. Brain Research Laboratories, New York Medical College, New York, NY **Evoked potentials in hyperkinetic and normal children under certainty and uncertainty: a placebo and methylphenidate study.** Psychophysiology. 13(5):419-428, 1976.

Differences between hyperkinetic children and normal children and the effects of methylphenidate on hyperkinetic children were investigated under conditions of differential attentional demands. Under conditions of certainty (low attention), in which the subject was told the identity of each stimulus in advance, few significant group differences were found. Treatment with methylphenidate normalized the evoked potentials of the hyperkinetic children, making them more like those of normal children. The findings are believed: 1) to reflect the deficit in attention observed behaviorally in hyperkinetic children; 2) to support a model of hypoarousal in hyperkinetic children; and 3) to reflect the behavioral normalization observed in hyperkinetic children treated with methylphenidate. 42 references. (Author abstract modified)

002831 Rey Mosquera, Jorge E.; Baron Cuervo, Luis Francisco; Ruiz Pelaez, Juan Gabriel. Departamento de Psiquiatria, Facultad de Medicina, Universidad Javeriana, Bogota, Columbia **/Electroencephalographic alterations in marihuana users./** Alteraciones electroencefalograficas en consumidores de marihuana. Revista Colombiana de Psiquiatria (Bogota). 5(4):410-430, 1976.

Following a review of recent literature on the effects of marihuana use, research aimed at finding the main neurotoxic effect of tetrahydrocannabinol (THC) in chronic users is presented. Electroencephalograms from 63 subjects (57 men, 6 women) were selected from a total of 6430 in the Columbian Neurological Foundation Institute according to the following criteria: 1) age 13 to 30 years; 2) patients who on the average had smoked at least 2 cigarettes per week for more than one year; 3) patients who had a hisotry of neurological disease or who were addicted to any other substance were eliminated.

The control group used was the percentage for electroencephalographic abnormality in the general normal population. Eighty one percent of the sample presented bioelectrical rhythm abnormality. Results are detailed according to age groups within the sample. EEG alterations chiefly consisted in slowed alpha rhythm, appearance of pathologic waves such as theta, and the appearance of paroxysmal complexes upon hyperventilation. The group of those who began smoking marihuana before age 15 is identified as a high risk group, presenting more pathologic tracings after greater length of use. Researchers and the public are alerted to the significant dangers of marihuana use, especially in the young. 10 references.

002832 Rotrosen, John; Angrist, Burton M.; Gershon, Samuel; Sachar, Edward J.; Halpern, Frieda S. Neuropsychopharmacology Research Unit, Dept. of Psychiatry, New York Univ. School of Medicine, 550 First Avenue, New York, NY 10016 **Dopamine receptor alteration in schizophrenia: neuroendocrine evidence.** Psychopharmacology (Berlin). 51(1):1-7, 1976.

Growth hormone (hGH) responses to apomorphine and L-DOPA were used as indices of CNS dopaminergic function in order to test hypotheses implicating dopaminergic alteration in the etiopathology of schizophrenia. Both drugs produced elevations in plasma hGH in both schizophrenics and controls. Unusually high hGH response to apomorphine was seen in schizophrenics who subsequently failed to respond to neuroleptic therapy; intermediate hGH response was seen in controls; and low hGH response was seen in subsequent neuroleptic responders. No such differences were seen in response to L-DOPA. It is suggested that the variability of hGH response to apomorphine is a reflection of dopamine receptor sensitivity, and that this variability may be an index of nonendocrine related dopaminergic sensitivity. The results are consistent with hypotheses relating schizophrenia to alteration in dopamine receptors. 26 references. (Author abstract modified)

002833 Sabelli, H. C.; Borison, R. L. Department of Pharmacology, Chicago Medical School, 2020 West Ogden Avenue, Chicago, IL 60612 **2-Phenylethylamine and other adrenergic modulators.** Advances in Biochemical Psychopharmacology. 15:69-74, 1976.

Studies leading to the phenylethylamine (PEA) theory of affective behavior, which holds that PEA is responsible for many of the ergotropic functions usually attributed to brain catecholamines, are reviewed. Endogenous PEA has been identified in human, rabbit, and mouse brain as well as peripheral tissues. It has been demonstrated that most of the behavioral and electrophysiological effects of PEA are not mediated by catecholamine release. Studies in humans and in animals have revealed that urinary excretion of PEA is decreased in depressed patients and that there is a fairly consistent relationship between affective changes induced by various drugs in man and their effects on the brain PEA content of animals. Agents causing depression in man reduce brain PEA content, while drugs which antagonize these effects (i.e. monoamine oxidase inhibitors, tricyclic antidepressants, mood elevating drugs such as alcohol and delta-9-tetrahydrocannabinol, L-DOPA, and CNS stimulants such as amphetamines) and electroshock increase brain PEA. It is suggested that PEA functions as a neuromodulator rather than as a neurotransmitter, and that PEA may serve to coordinate central and peripheral adrenergic functions. 20 references.

002834 Sacchetti, E.; Smeraldi, E.; Cagnasso, M.; Biondi, P. A.; Bellodi, L. Department of Psychiatry, Milan University School of Medicine, Via F. Sforza 35, I-20122 Milan, Italy **MHPG, amitriptyline and affective disorders: a longitudinal study.** International Pharmacopsychiatry (Basel). 11(3):157-162, 1976.

The daily urinary excretion of 3-methoxy-4-hydroxyphenylglycol (MHPG) was studied in five male depressed patients before and during a 4 week treatment with amitriptyline, to determine whether urinary excretion of this compound could serve as a suitable indicator of changes in the metabolism of norepinephrine in the brain. The patients were followed during a pretreatment period and then during a treatment period in which amitriptyline was administered. The data suggest that: 1) there is a wide individual variability of MHPG pretreatment levels; 2) amitriptyline modifies MHPG levels in a way which seems to be related to the pretreatment MHPG; 3) amitriptyline may produce a sustained improvement in depressive symptoms, independent of the pretreatment MHPG values; and 4) the time course of modifications in MHPG excretion is shorter than the time course of clinical improvement. It is concluded that the data do not support the catecholamine hypothesis, which postulates a direct linkage between catecholamine metabolism and affective disorders. Rather, the data strengthen the work hypothesis of a more complex chain of biochemical abnormalities underlying the disorders of mood, with abnormalities of the catecholaminergic system acting only as a link in this complex. 32 references. (Author abstract modified)

002835 Sedvall, G.; Alfredsson, G.; Bjerkenstedt, L.; Eneroth, P.; Fyro, B.; Harnryd, C.; Swahn, C. -G.; Wiesel, F. -A.; Wode-Helgodt, B. Division of Neuropsychopharmacology, Department of Pharmacology, Karolinska Institutet, S-10401 Stockholm, Sweden **Selective effects of psychoactive drugs on levels of monoamine metabolites and prolactin in cerebrospinal fluid of psychiatric patients.** In: Airaksinen, M., CNS and behavioural pharmacology. Elmsford, New York, Pergamon Press, 1976. 344 p. v. 3. (p. 255-267).

In a paper presented at the Sixth International Congress of Pharmacology held in Helsinki, Finland in July, 1975, studies of the selective effects of psychoactive drugs on the levels of monoamine metabolites and prolactin in the cerebrospinal fluid (CSF) of psychiatric patients are reported. A procedure for the simultaneous determination of homovanillic acid (HVA), 5-hydroxyindoleacetic acid (5-HIAA), and 3-methoxy-4-hydroxyphenylethyleneglycol (MOPEG) (metabolites of dopamine (DA), serotonin (5-hydroxytryptamine, 5-HT), and noradrenaline (NA), respectively), in CSF is described. Studies of the effects of various drugs on the levels of monoamine metabolites in the CSF of psychotic patients revealed that: 1) chlorpromazine or thiothixene, and to a lesser extent, methylperone, elevate the HVA level; 2) none of the antipsychotic drugs has a significant effect on the 5-HIAA level; 3) lithium increases both 5-HIAA and HVA levels; 4) chlorimipramine decreases the 5-HIAA level but has no significant effect on HVA levels; and 5) chlorpromazine substantially reduces the MOPEG level. The data are generally in agreement with those obtained in the brains of experimental animals and demonstrate the specificity and diversity of biochemical effects of each type of psychoactive drug on transmitter metabolism in the human CNS. The effects of psychoactive drugs on prolactin like immunoreactivity in ventricular and lumbar CSF of patients have also been studied and it is reported that chlorpromazine, thiothixene, and methylperone elevate the prolactin level in the CSF of psychotic patients and that lithium or chlorimipramine have no significant effect on the prolactin level of manic-depressive patients. Correlations between

plasma levels and CSF levels of chlorpromazine are also discussed and it is suggested that study of the relationship between drug concentrations in the CNS of psychiatric patients and their antipsychotic effect may be possible. 31 references.

002836 Sedvall, G.; Alfredsson, G.; Bjerkenstedt, L.; Eneroth, P.; Fyro, B. Harnryd, C.; Swahn, C.-G.; Wiesel, F.-A.; Wode-Helgodt, B. Department of Pharmacology, Karolinska Institutet, S-10401 Stockholm, Sweden **Selective effects of psychoactive drugs on levels of monoamine metabolites and prolactin in cerebrospinal fluid of psychiatric patients.** Research report, NIMH Grant MH-27254, 1976. 13 p.

A mass fragmentographic methodology for the determination of major monoamine metabolites in human cerebrospinal fluid was described, and results of a study of the selective effects of psychoactive drugs on monoamine metabolite and prolactin levels in the cerebrospinal fluid (CSF) of psychiatric patients were presented. Tabular data on the effects of chlorpromazine, thiothixene, methylperone, lithium, and chlorimipramine on the levels of homovanillic acid (HVA), 5-hydroxyindoleacetic acid (5-HIAA) and prolactin in CSF are presented which indicate specific effects on brain monamine metabolism. CSF levels of 3-methoxy-4-hydroxyphenylethyleneglycol (MOPEG) may also be markedly affected by psychoactive drug treatment. It is suggested that by using mass fragmentography and radioimmunoassay it is possible to use the CSF of psychiatric patients as a tool for quantitative biochemical studies. It is concluded that by correlating biochemical, pharmacokinetic, and clinical data, the intricate relationships between psychopathology, brain biochemistry, and pharmacokinetics may be elucidated. 31 references.

002837 Sen, Amar K.; Awad, Awad Girgis; Stancer, Harvey C.; Godse, Damodar D. Department of Pharmacology, University of Toronto, Toronto M5S 1A8, Canada **Urinary cyclic AMP in relation to lithium treatment in manic-depressive illness.** Journal of Nervous and Mental Disease. 163(3):210-213, 1976.

In a longitudinal study, changes in 24 hr urinary excretion of cyclic adenosine monophosphate (AMP) in six manic depressives of the bipolar type were compared before and during lithium treatment. The values varied from 3.55 to 19.0mumol/24 hr with considerable variation between subjects. Three of these patients improved with administration of lithium carbonate. This improvement was not correlated with a change in cyclic AMP excretion. Five normal male volunteers were studied over a five day period. The urinary excretion for this group showed the same large intersubject variability but smaller intrasubject variation as was found for the patient group. It is suggested that erroneous results may be obtained for urinary cyclic AMP excretion if mean group values are used from patients not studied longitudinally. 18 references. (Author abstract modified)

002838 Stillman, Richard; Galanter, Marc; Lemberger, Louis; Fox, Sherman; Weingartner, Herbert; Wyatt, Richard Jed. Division of Special Mental Health Research, IRP, NIMH, St. Elizabeth's Hospital, Washington, DC 20032 **Tetrahydrocannabinol (THC): metabolism and subjective effects.** Life Sciences (Oxford). 19(4):569-576, 1976.

Research data are presented on the relationships between plasma levels of delta9-THC and its metabolites and changes in pulse rate and subjective reports following smoking of a marihuana cigarette. C-14 labeled delta9-THC was administered in spiked cigarettes to nine experienced marihuana smokers. Blood samples obtained by repeated venipuncture showed that the Ss' subjective estimates of being high appeared to parallel the blood concentration of THC metabolites at least as closely as the blood concentration of THC itself. After 30 min, subjective effects declined less rapidly than either THC or its metabolites. Substantial interindividual consistency in THC concentrations was found, suggesting that administration of THC in cigarettes under standardized smoking conditions can produce reliable blood concentrations of THC. A second session was run with the same Ss, this time omitting venipuncture, and using unlabeled THC. Significant differences between the effects of initial doses of THC under stress and no stress conditions appeared in the detailed subjective effects inventories provided by subjects. 15 references. (Author abstract modified)

002839 Sulman, F. G.; Pfeifer, Y.; Tal, E. Hebrew University, Hadassah Medical School, Jerusalem, Israel **Effect of enzyme induction by barbiturates on neurohormone excretion in man.** Israel Journal of Medical Sciences (Jerusalem). 12(12):1521, 1976.

A summary of a paper delivered at the 35th meeting of the Israel Physiological and Pharmacological Society on the effect of enzyme induction by barbiturates on neurohormone excretion in man is presented. The effectiveness of proxibarbital on the neurohormone profile of 25 patients is noted. Multiple enzyme induction which normalizes neurohormone production, metabolism, and excretion is accomplished by increasing monoamine oxidase activity which destroys surplus serotonin adrenaline and noradrenaline; augmenting diamine oxidase activity which destroys surplus of histamine; and activating decaroxylases and dehalogenases which destroy surplus of thyroxine and its derivatives. The use of proxibarbital for the treatment of suitable cases of migraine, serotonin abortion, hypertension, allergy, and hyperthyroidism is indicated.

002840 Tilkian, Ara G.; Schroeder, John S.; Kao, John Jue; Hultgren, Herbert N. Psychiatry Division, Veterans Administration Hospital, Palo Alto, CA 94305 **The cardiovascular effects of lithium in man: a review of the literature.** American Journal of Medicine. 61(5):665-670, 1976.

The medical literature since 1900 is reviewed to determine the nature of lithium's cardiovascular effects. In therapeutic doses, lithium produced reversible T-wave flattening and inversion in the electrocardiogram; rarely, it may cause sinus node dysfunction or ventricular arrhythmias. Patients with lithium toxicity almost always present with neurologic signs and symptoms. "Hypotension and cardiovascular collapse," alleged cardiotoxic manifestations of lithium, invariably follow days of coma. Given the possible cardiotoxic effect of other psychopharmacologic agents and the hazards of withholding effective therapy in mania, it is concluded that lithium may be used safely in patients with cardiac disease if the dose is adjusted to the rate of lithium excretion and if serum levels of lithium are followed carefully. When used in patients with cardiac arrhythmias, frequent electrocardiographic monitoring is advised. 66 references. (Author abstract)

002841 van Praag, H. M.; Korf, J. Department of Biological Psychiatry, Psychiatric University Clinic, Groningen, The Netherlands **Importance of the dopamine metabolism for the clinical effects and side effects of neuroleptics.** In: Airaksinen, M., CNS and behavioural pharmacology. Elmsford, New York, Pergamon Press, 1976. 344 p. v. 3. (p. 299-307).

In a paper presented at the Sixth International Congress of Pharmacology held in Helsinki, Finland in July, 1975, a study

of the relationship between human central dopamine (DA) metabolism and the clinical effects of neuroleptics (haloperidol, chlorpromazine or perphenazine) in patients with acute psychoses is reported. The neuroleptic induced increase in central DA turnover, as an indicator of the degree of DA receptor blockade, was positively correlated with the therapeutic effects of the drugs as well as to the development of hypokinetic/rigid side-effects. It was also found that: 1) neuroleptics of different chemical structure do not significantly differ in their intrinsic ability to produce hypokinetic/rigid symptoms; 2) development of these symptoms depends on the patient's individual susceptibility; and 3) the individual susceptibility is based on a relatively low DA turnover. The data support the view that DA antagonism is related to the clinical effects as well as the side-effects of neuroleptics. 22 references. (Author abstract)

002842 Viala, A. Laboratoire de Toxicologie generale et Biotoxicologie, Faculte de Pharmacie, 27, boulevard Jean-Moulin, F-13005 Marseilles, France /**Pharmacokinetic profile of perphenazine enanthate.**/ Sur le profil pharmacocinetique de l'enanthate de perphenazine. Encephale (Paris). 2(3):273-282, 1976.

The literature on blood kinetics, biotransformation, excretion, and tissue distribution of perphenazine enanthate is reviewed. After i.m. injection of the drug in man, metabolic products may be rapidly retrieved from the blood during the first few hours. A maximum blood level is obtained after 0.5to 3.5days, which then shows a slow, progressive decrease during the following days. When 100mg was administered, the curve reached 0 before the 15th day only in two of eight cases, reaching 0 on the 10th and 14th days, respectively. Good efficacy without side-effects seems to be obtained with a plasma level of 0.5to 7mcg/1. The principal metabolites of perphenazine enanthate are perphenazine, perphenazine sulfoxide, hydroxyperphenazine, piperazinyl-10-chlor-2'-phenothiazine, and a glucuronide. 21 references.

002843 Vohland, H.-W.; Hadisoemarto, S.; Wanke, B. Institut fur Toxikologie und Pharmakologie der Phillipps-Universitat, Pilgrimstein 2, D-3550 Marburg, Germany /**On the toxicology of carbromal.**/ Zur Toxikologie von Carbromal. Archives of Toxicology (Berlin). 36(1):31-42, 1976.

The toxic effects of carbromal were analyzed in order to estimate its hypnotically active metabolites in rats and humans. The absorption and elimination of carbromal including biotransformation of carbromal to bromethylbutyramide and ethylbutyrylurea were studied in rats. Both metabolites, significant amounts of which were found in serum and brain, distributed evenly, as did carbromal. Carbromal was given orally to 4 humans and highest serum concentrations were found 30 min after ingestion, declining rapidly thereafter. Parallel determination of total bromide in rat tissues and in human serum showed that the concentrations of the hypnotically active compounds declined rapidly while inorganic bromide was eliminated more slowly. 37 references. (Author abstract modified)

002844 Walinder, Jan; Skott, Annika; Carlsson, Arvid; Nagy, Adam; Roos, Bjorn-Erik. University of Goteborg, Goteborg, Sweden **Potentiation of the antidepressant action of clomipramine by tryptophan.** Archives of General Psychiatry. 33(11):1384-1389, 1976.

Clomipramine (chlorimipramine) was studied with and without concomitant tryptophan in a double-blind taial in 26 consecutive female admissions suffering from endogenous depression. The patients, 17 to 71 years old, all had unipolar depression. the depressives were given a fixed dosage of 50mg t.i.d. clomipramine for 3 weeks. The tryptophan group received a daily dosage of 0.1mg/kg DL-tryptophan and the other group received placebo tablets. In each group, 12 patients completed the trial. Depression and anxiety symptoms decreased more markedly in the clomipramine tryptophan group than in the clomipramine/placebo group, while retardation decreased similarly in both groups. Sleep disturbances decreased significantly only in the placebo group. Plasma levels of clomipramine reached a plateau within a few days, whereas the level of the monodesmethyl metabolite of clomipramine continued to rise and reach considerably higher values than the parent compound. Plasma levels and cerebrospinal fluid levels of tryptophan were elevated threefold in afternoon samples in the tryptophan group. The cerebrospinal fluid level of 5-hydroxyindoleacetic acid decreased by half, and homovanillic acid increased 50% in the tryptophan group. The latter showed no change in the placebo group. Good responders showed higher levels of clomipramine plus desmethylchlorimipramine than did poor responders. 22 references.

002845 Weinstock, M.; Shoham-Moshonov, S. Sackler School of Medicine, Tel Aviv, Israel **Seasonal variation in development of tolerance to morphine.** Israel Journal of Medical Sciences (Jerusalem). 12(12):1521, 1976.

A summary of a paper delivered at the 35th meeting of the Israel Physiological and Pharmacological Society on the seasonal variation in the development of tolerance to morphine is presented. It was noted that tolerance of morphine seemed higher in summer than in winter. A number of factors involved in morphine tolerance which were observed are: size of the response of the muscle to coaxial stimulation, sensitivity of the muscle to exogenous acetylcholine (AC), sensitivity of the muscle to morphine, and the AC output per stimulus and its inhibition by morphine. Tissue was found to be significantly less sensitive to exogenous AC in summer months, and the contractions induced by coaxial stimulation were also smaller. In the winter months morphine blocked the effect of AC on the muscle in addition to inhibiting AC release.

002846 Wielosz, Marian; Salmona, Mario; de Gaetano, Giovanni; Garattini, Silvio. Department of Pharmacology, Institute of Clin. Pathology, Medical School, Lublin, Poland **Uptake of 14C-5-hydroxytryptamine by human and rat platelets and its pharmacological inhibition: a comparative kinetic analysis.** Naunyn-Schmiedeberg's Archives of Pharmacology (Berlin). 296(1):59-65, 1976.

In order to approach the uptake of (14C-5-hydroxytryptamine) by platelets as a first order process, a kinetic model was used to evaluate the relative potency and the type of inhibition of 14C-5HT uptake exhibited by imipramine, chlorimipramine and Fenfluramine. All 3 compounds inhibited 14C-5-HT uptake by platelets. Chlorimipramine was about 10 times more effective than imipramine both in rat and in human platelets. Both drugs were more potent inhibitors on human than on rat platelets. Fenfluramine was almost as active as imipramine on rat but 30 times less potent than imipramine on human platelets. Both imipramine and chlorimipramine inhibited 14C-HT uptake by an apparent noncompetitive mechanism, whereas Fenfluramine appeared to act as a competitive inhibitor. No differences were found in this respect between human and rat platelets. Pharmacological or therapeutic doses of these drugs usually result in plasma concentrations similar to those found in this study to effectively inhibit platelet 14C-HT uptake.

002847 Yamauchi, Michi. Department of Neuropsychiatry, Kurume University School of Medicine, Kurume and Kai Hospital, Yanagawa, Japan **Effects of L-Dopa and vitamin B6 on electroencephalograms of schizophrenic patients: a preliminary report.** Folia Psychiatrica et Neurologica Japonica (Tokyo). 30(2):121-151, 1976.

The effects of L-Dopa and vitamin B-6, alone and in combination, on symptomatic improvement and associated electroencephalographic (EEG) changes were assessed in patients with chronic schizophrenia. L-Dopa alone produced practically no symptomatic improvement or EEG changes. Vitamin B-6 (as pyridoxal-5'-phosphate) produced little symptomatic improvement but brought about EEG changes suggestive of an ameliorative effect. Combined treatment with L-Dopa and vitamin B-6 produced both symptomatic improvement and EEG improvement. It is suggested that diminution of the activity of decarboxylase essential to the metabolsim of L-Dopa to dopamine may be present in chronic schizophrenic patients. 35 references. (Author abstract modified)

14 MECHANISM OF ACTION: BEHAVIORAL

002848 Adam, Kirstine; Adamson, Liisi; Brezinova, Vlasta; Hunter, William M.; Oswald, Ian. Sleep Laboratory, University Department of Psychiatry, Royal Edinburgh Hospital, Edinburgh EH10.5HF, Scotland **Nitrazepam: lastingly effective but trouble on withdrawal.** British Medical Journal (London). No. 6025:1558-1560, 1976.

The sleep of ten volunteers with an average age of 57 years was recorded electrophysiologically before, during, and after nitrazepam 5mg nightly for 10 weeks. Sleep was longer and less broken on the drug and no tolerance was obvious after 2 months use. Withdrawal of the drug, however, caused sleep to be temporarily worse than before the drug had been taken. Slow-wave sleep was reduced by nitrazepam, but the accompanying secretion of growth hormone was not impaired. 20 references. (Author abstract modified)

002849 Autret, A.; Minz, M.; Bussel, B.; Cathala, H. P.; Castaigne, P. Clinique des Maladies du Systeme Nerveux, 47, boulevard de l'Hopital, 75634 Paris Cedex 13, France **Human sleep and 5-HTP: effects of repeated high doses and of association with benserazide (RO.04.4602).** Electroencephalography and Clinical Neurophysiology (Amsterdam). 41(4):408-413, 1976.

A single-blind study was designed to investigate the effects of large doses of DL-5-hydroxtryptophan (DL-5-HTP) administered orally, alone or with benserazide -- a decarboxylase inhibitor -- on the sleep of normal human subjects and to help clarify apparent contradictions in results noted after administration of precursors of serotonin in human and animal studies. DL-5-HTP or a placebo was administered to 3 healthy male volunteers in a schedule of placebo (1 week), 5-HTP (2 weeks), and placebo again (9 days); in 2 of the subjects, benserazide was added to the 5-HTP dosage for the last 2 days of active drug treatment. The paradoxical sleep time and percentage tended to show a decrease during the 2nd week of treatment, followed by a rebound effect after the end of treatment. Similar results were obtained when 5-HTP was administered together with benserazide. 14 references.

002850 Babor, Thomas F.; Mendelson, Jack H.; Kuehnle, John. Alcohol and Drug Abuse Research Center, Harvard Medical School, McLean Hospital, Belmont, MA 02178 **Marihuana and human physical activity.** Psychopharmacology (Berlin). 50(1):11-19, 1976.

The physical activity of 26 adult male volunteers with a prior history of either moderate or heavy marihuana use were systematically observed before, during, and after a 21 day period of free access to delta9-tetrahydrocannabinol marihuana cigarettes. A matched sample of 11 casual alcohol drinkers served as a control group. Sleep and other molar behaviors were observed hourly to obtain a representative sample of daily activity. Both moderate and heavy users were less active immediately after marihuana use and slept more on days following heavier consumption. Heavy users reduced their waking activity on days following heavier consumption, as well as during the entire period of marihuana availability. These reactions did not persist beyond the period of availability for either group. The findings suggest a dose related delayed reaction to heavy marihuana consumption which disappears following the cessation of regular use. However, changes in activity following single doses of marihuana may be related more to the social circumstances of its use than to its pharmacological action. 29 references. (Author abstract modified)

002851 Ban, Thomas A.; Pecknold, John C. no address **Haloperidol in the therapy of severe behavior disorders.** Current Psychiatric Therapies. 16:127-137, 1976.

Uses of the psychoactive butyrophenone preparations, including haloperidol and droperidol, are reviewed. The use of haloperidol in children's behavior disorders is described. Behavior disorders in adults treated with butyrophenones include those associated with addiction, sexual deviation, neuroses, schizophrenia, mania, Gilles de la Tourette's syndrome, and organic brain syndromes. Adverse effects are outlined. In the initial publications it was suggested that butyrophenones exert their therapeutic effects by occupying gamma-aminobutyric acid receptors, or by their cell membrane permeability decreasing effect. During the 1960's a positive relationship was also revealed between the postsynaptic dopamine receptor blockade and therapeutic effects in Huntington's chorea, Gilles de la Tourette's disease, schizophrenia, and mania. Despite the common contention that haloperidol should be used exclusively for the treatment of functional psychoses, it has been demonstrated that haloperidol can be used effectively in the treatment of behavior disorders of children, adults, and geriatric patients. Among the other butyrophenones, benzperidol was found to be therapeutically effective in behavior disorders associated with sexual deviation, and droperidol was found beneficial in mania. 66 references. (Author abstract modified)

002852 Barkley, Russell A. Child Development and Rehabilitation Center, University of Oregon Health Sciences Center, Portland, OR 97201 **Predicting the response of hyperkinetic children to stimulant drugs: a review.** Journal of Abnormal Child Psychology. 4(4):327-348, 1976.

Thirty six research reports involving more than 1400 hyperkinetic children in an effort to determine variables that have proven useful in predicting which hyperkinetic children will respond favorably to stimulant drugs are reviewed. The research is summarized under eight types of predictor variables: 1) psychophysiological; 2) neurological; 3) familial, 4) demographic/sociological; 5) diagnostic category; 6) parent/teacher/clinician rating; 7) psychological; and 8) profile types. Results indicate that, to date, measures of attention span or concentration and its correlates have proven to be the most useful predictors of the response of hyperactive children to drugs. The results also suggest that hyperkinetic children are heterogeneous with respect to levels of central nervous system arousal and that this variable may prove useful in pre-

dicting their response to stimulant drugs. 55 references. (Journal abstract modified)

002853 Boehringer Ingelheim Ltd., 33 West Tarrytown Rd., Elmsford, NY 10523 (914-592-4311). BOE **Case Studies in Psychiatric Management: Hospital to Community.** 16mm optical Color 25 min, 1976.

Cases illustrating four types of disorders treated by medication in combination with other therapies is presented. The first patient, diagnosed a chronic schizophrenic, thought his parents were the Mafia. Next presented is a hyperactive geriatric patient with organic brain syndrome who seems to be in constant torment. Another patient is a psychoneurotic woman who unconsciously swallows air to simulate a gastric disorder. Finally, there is an overly aggressive mentally retarded boy who acts out his hostilities toward his mother. In each case the patients are viewed before, during, and after successful drug therapy. Primary function of film is to explain to psychiatrists and physicians the qualities of phenothiazine.

002854 Bulpitt, C. J.; Hoffbrand, B. I.; Dollery, C. T. Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine, Keppel Street, London WCl 7HT, England **Psychological features of patients with hypertension attending hospital follow-up clinics.** Journal of Psychosomatic Research (Oxford). 20(5):403-410, 1976.

To determine whether treatment with certain hypotensive drugs causes a psychological abnormality, 946 patients with hypertension who were receiving treatment at two hospital clinics were given a slightly modified Middlesex Hospital Questionnaire, which assesses general neurotic illness and rates patients in terms of the following categories: free floating anxiety, phobic anxiety, depression, obsessionality, somatic complaints, and hysteria. Compared with previous findings for the general population, the hypertensive patients scored significantly higher for free floating anxiety, phobic anxiety, and depression. Further, male hypertensive patients, but not female patients, scored higher for obsession and hysteria. It is suggested that the high scores for hypertensive patients could not be closely correlated with any particular drug therapy, with the exception of phobic anxiety and propranolol in women. Also, a weak, but statistically significant correlation was found between systolic blood pressure and both somatic complaint rate and phobic anxiety. It is concluded that because an excessive proportion of treated hypertensive patients had abnormal psychoneurotic scores, it is possible that the treatment situation leads to psychoneurosis or that selection by the doctor or patients results in a biased hospital population containing an excess of neurotic patients. Studies on small numbers of the general population suggest that selection may be important. 26 references. (Author abstract modified)

002855 Carlsson, Carl. Nordhemspolikliniken, Goteborg, Sweden **Propranolol in alcoholism.** In: Carlsson, C., Neuropsychiatric effects of adrenergic beta-receptor. Munich, Urban & Schwarzenburg, 1976. 120 p. (p. 53-57).

In a paper presented to a symposium on neuropsychiatric effects of adrenergic beta-receptor blocking agents held at Copenhagen, October 1975, controlled studies and broad clinical experience are cited showing that propranolol, in a number of cases, is a suitable drug in alcoholism treatment, especially as there is no risk of habituation. It is asserted that the reason why propranolol has beneficial effects on chronic alcoholics can only be a matter of speculation. It is thought that since euphoria from amphetamine and alcohol have much in common and can be blocked by the same substances, both may act in the functional unit, the so called rewarding center; and that beta-receptors or related mechanisms might in some way be involved in this process, possibly as feedback mechanisms. 15 references.

002856 Casado, Dario. 61 East 86th Street, New York, NY 10028 **/Effects of some psychoactive drugs upon the trapezoid illusion perception./** Effectos de algunas drogas psicoactivas sobre la percepcion de la illusion del trapezoide. Revista Latinoamericana de Psicologia (Bogota). 8(1):15-24, 1976.

The trapezoid illusion discovered by Ames was investigated on ten male subjects under the effect of several psychopharmacologic drugs: dextroamphetamine sulfate, 5mg; meprobamate, 400mg; pentobarbital sodium, 50mg. The experiment took place in a dark room. There were 12 sessions of 4 hours each during which the stimulus target was presented rotating and oscillating for 3 min every 30 min. The number of perceived illusions was higher when the target rotated; they increased with pentobarbital, and decreased with dextroamphetamine. 5 references. (Author abstract modified)

002857 Chesher, G. B.; Franks, H. M.; Hensley, V. R.; Hensley, W. J.; Jackson, D. M.; Starmer, G. A.; Teo, R. K. C. Department of Pharmacology, University of Sydney, New South Wales 2006, Australia **The interaction of ethanol and delta9-tetrahydrocannabinol in man: effects on perceptual, cognitive and motor functions.** Medical Journal of Australia (Glebe). 2(5):159-163, 1976.

The interaction of ethanol and delta9-tetrahydrocannabinol (THC) was examined in terms of their effects on perceptual, cognitive, and motor functions related to driving ability in 12 subjects. In a double-blind crossover experiment, each drug was administered in a dose considered to be in the moderate or social range, alone and in combination with the other. Both THC and ethanol had little effect when administered alone. The combination of drugs, however, induced a significant decrement in performance in some of the tests and this interaction was considered to be at least additive. The peak blood ethanol concentration was higher when subjects received both ethanol and THC than when they received ethanol alone. 18 references. (Author abstract modified)

002858 Crawford, W. A.; Franks, H. M.; Hensley, V. R.; Hensley, W. J.; Starmer, G. A.; Teo, R. K. C. Fisons Pty, Ltd., Sydney, Australia **The effect of disodium cromoglycate on human performance, alone and in combination with ethanol.** Medical Journal of Australia (Glebe). 1(26):997-999, 1976.

The effect of disodium cromoglycate (DSCG, used to treat asthma and rhinitis) on human performance, alone and in combination with ethanol, was studied in 17 subjects. A double-blind crossover experiment investigated effects on manual dexterity, numerical reasoning, and perceptual speed. DSCG had little effect on performance when administered alone. When administered with ethanol, DSCG did not significantly modify the ethanol induced decrement in performance except in the complex reaction time test. Reasons for the findings are suggested, and the importance of awareness of the interactive effects of drugs with social drinking is emphasized. 5 references. (Author abstract modified)

002859 Einspruch, Burton C. 3707 Rawlins, Dallas, TX 75219 **Helping to make the final years meaningful for the elderly residents of nursing homes.** Diseases of the Nervous System. 37(8):439-442, 1976.

Hydergine was tested as a therapeutic agent to help reduce the severity of loss of hope, loss of self-confidence, lack of interest in life, and eventually loss of all contact with reality in elderly people. It is concluded that Hydergine sublingual tablets are a useful therapeutic agent for the relief of select symptoms seen in the elderly. The patients receiving this drug showed the greatest improvement in 17 of the 18 symptoms rated in this study. By relieving those symptoms commonly seen in the elderly such as, mood depression, confusion, unsociability, dizziness, and impaired self-care, many elderly residents can be encouraged and enabled to take a more active part in rehabilitative programs and social activities of the nursing home and thereby help make their final years more meaningful. 7 references.

002860 Flynn, Nona Mitchell. George Washington University, Washington, DC 20006 **The effect of positive teacher reinforcement and classroom social structure on class behavior of boys diagnosed as hyperactive before and during medication. (Ed.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-23546 HC$15.00 MF$8.50 293 p.

A descriptive study of 42 hyperactive boys' behavior with and without medication examined two aspects of the natural learning environment (emotional climate with use of positive teacher reinforcement and classroom structure as teacher centered or pupil centered). Under normal learning conditions the classrooms were rated in regard to these two factors and related to the level of children's hyperactive behaviors. Environmental factors were measured by an observation schedule and record, and hyperactive behaviors were measured by teachers' ratings. The tested hypotheses indicated that positive teacher reinforcement was an important factor in reducing hyperactivity when subjects were medicated. The measure of social structure in relationship to hyperactivity was not significant, but the environment of the pupil centered classroom was positively related to the use of reinforcement. Implications for teacher training, classroom environment, and for a new educational specialization were discussed. (Journal abstract modified)

002861 Gittelman-Klein, Rachel; Klein, Donald F.; Katz, Sidney; Saraf, Kishore; Pollack, Edith. Long Island Jewish-Hillside Medical Center, PO Box 38, Glen Oaks, NY 11004 **Comparative effects of methylphenidate and thioridazine in hyperkinetic children.** Archives of General Psychiatry. 33(10):1217-1231, 1976.

The effects of three pharmacological treatments, methylphenidate hydrochloride thioridazine hydrochloride, a methylphenidate/thioridazine combination, and placebo were studied in outpatient hyperkinetic children rated hyperactive both in school and at home or clinic. Though initially the combination of methylphenidate and thioridazine tended to produce greater clinical improvement it was not superior to methylphenidate alone after 12 weeks of treatment. Methylphenidate alone and the methylphenidate/thioridazine combination were more effective than thioridazine alone. 19 references. (Author abstract)

002862 Gittelman-Klein, Rachel; Klein, Donald F.; Abikoff, Howard; Katz, Sidney; Gloisten, Audrey C.; Kates, Wendy. Dept. of Psychiatry, Long Island Jewish-Hillside Medical Center, Glen Oaks, NY 11004 **Relative efficacy of methylphenidate and behavior modification in hyperkinetic children: an interim report.** Journal of Abnormal Child Psychology. 4(4):361-379, 1976.

Children reported to be hyperactive in school and with behavior difficulties at home were randomly assigned to methylphenidate, behavior therapy and placebo, or behavior therapy with methylphenidate for an 8 week period. Rating scales were obtained from teachers and parents and independent blind observers rated children's classroom behavior on a weekly basis. A behavior therapy program was implemented in the home and at school. Methylphenidate dosage was individualized. Ratings of behavior deviance were significantly reduced by all treatments. However, a significant advantage for the groups receiving methylphenidate was found over the group receiving behavior therapy and placebo. No significant differences were found between methylphenidate alone and methylphenidate combined with behavior therapy. Global ratings of improvement by teachers favored the combined treatment of behavior therapy and methylphenidate over behavior therapy and placebo. No differences among treatments were found in the mothers' global ratings of improvement. Results indicate that though all three treatments were effective, methylphenidate was significantly superior to behavior therapy alone. 28 references. (Journal abstract modified)

002863 Halliday, Roy; Rosenthal, Joseph H.; Naylor, Hilary; Callaway, Enoch. University of California, Langley Porter Neuropsychiatric Institute, San Francisco, CA 94143 **Averaged evoked potential predictors of clinical improvement in hyperactive children treated with methylphenidate: an initial study and replication.** Psychophysiology. 13(5):429-440, 1976.

In two experiments certain measures of the visual evoked potential (VEP) discriminated between hyperactive children who were subsequently judged by their pediatrician to have shown significant improvement (responders) with methylphenidate (Ritalin) as compared to children who showed a poor or marginal response to this drug. The principal findings were: 1) with Ritalin, EP variability increased when responders went from a task requiring active attention (ATT) to one requiring passive observing (PAS): in contrast, EP variability decreased in nonresponders when they went from ATT to PAS; 2) the amplitude of the N140 P190 component in the ATT condition increased from placebo to Ritalin for the responders. It was suggested that the variability measure primarily reflects an abnormalizing effect of Ritalin on the nonresponder while the N140 P190 component represents an apparent deficit in responders that is normalized by Ritalin. 27 references. (Author abstract)

002864 Heimann, H. Centre de recherche psychopathologique, Clinique psychiatrique universitaire de Lausanne, Switzerland /**The effect of psychotropic drugs on the normal subject and their importance for the prediction of clinical effects.**/ L'effet des medicaments psychotropes sur le sujet normal et son importance pour la prediction des effets cliniques. In: Advances in the drug therapy of mental illness. Geneva, World Health Organization, 1976. 168 p. (p. 69-78).

The effect of psychotropic drugs on the normal subject and their importance for the prediction of clinical effects is discussed. Research in this area complements basic research in neuropharmacology, biochemistry, and psychopharmacology. It is concluded that: 1) too much attention is being given to clinical symptoms; 2) too few studies have dealt with the depression syndrome from the psychophysiological viewpoint of the theory of activation; 3) the different forms that the syndrome takes goes from psychomotor inhibition to anxious agitation; and 4) the way to view the syndrome should be viewed according to the activation theory. 24 references.

002865 Koranyi, E. K. Department of Psychiatry, Ottawa General Hospital, 197 Cumberland Street, Ottawa, Ontario,

Canada **Remarkable etiology in a case of Gilles de La Tourette's disease.** Psychiatric Journal of the University of Ottawa (Ottawa). 1(1-2):5-7, 1976.

Implications for etiology and treatment of classical Gilles de La Tourette's disease are suggested in the case history of a 16-year-old boy. At 10 years of age the child developed facial tics, involuntary grunting noises, and coprolalia 5 months after self-discovered addiction to inhaling gasoline. Typical scalp EEG changes and organic signs such as borderline dull/normal intelligence and poor psychomotor coordination were demonstrated on psychological testing. The patient failed to respond to low doses of haloperidol and refused to continue higher doses because of extrapyramidal side effects. Chlorazepate dipotassium was given with good effect, supporting the potential usefulness of this drug in some cases of Gilles de La Tourette's disease. 18 references. (Author abstract modified)

002866 Meyer, Jon K. Sexual Behaviors Consultation Unit, Johns Hopkins Medical Institutions, Baltimore, MD **Clinical management of sexual disorders.** Baltimore, Williams & Wilkins, 1976. 291 p. $16.00.

Recent findings regarding the approach to patients with sexual disorders, the diagnosis and classification of these disorders, the determination of significant variables in sexual conditions, and the application of selected treatment techniques are presented. While the emphasis is on direct manipulation and treatment techniques, the full range of treatment modalities considered includes: 1) formal psychoanalysis; 2) behavior modification and desensitization; 3) surgical intervention; 4) drug therapy; and 5) short-term conjoint sexual therapy. The nanagement of sexually dysfunctional patients with physical disorders is discussed, and drug induced alterations in human sexual function and research in animal sexual behavior are presented. It is asserted that no one treatment modality is sufficient to cover all possible sexual dysfunctions, and the practitioner must select the appropriate technique according to the patient's symptoms, lifestyle, interpersonal relationships, financial resources, and emotional health.

002867 Miller, Loren; Cornett, Terry; Brightwell, Dennis; McFarland, Dennis; Drew, William G.; Wikler, Abraham. Department of Psychiatry, University of Kentucky Medical Center, Lexington, KY 40506 **Marijuana and memory impairment: the effect of retrieval cues on free recall.** Pharmacology Biochemistry and Behavior. 5(6):639-643, 1976.

In an attempt to ascertain the effect of retrieval cues on recall deficits which occur following intoxication with marihuana, 40 male volunteers were presented with word lists following the smoking of a single 1g marihuana or placebo cigarette and then were required to recall these words immediately after presentation. Recall occurred under a condition in which cues representative of to be remembered words were present or in an uncued condition. Results indicated that recall was depressed following marihuana administration under both cued and uncued conditions with cues being only mildly effective in reversing the recall deficit. There was no increase in the number of internal intrusions under marihuana, but the number of external intrusions was significantly elevated under the cued condition. 25 references. (Author abstract)

002868 Osorio, Paulo Leo Manassi. University of Houston, Houston, TX 77004 **Automated analysis of EEG patterns in subjects under abusive levels of sedative-hypnotics. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-21864 HC$15.00 MF$8.50 324 p.

Statistical techniques, including spectral analysis, which are more sensitive to the variations in EEG waveforms than the classical approach of sleep staging were used to detect the possible effects of two sedative hypnotic agents (secobarbital and methaqualone) on the sleep EEGs of two groups of Ss. One group contained Ss who were withdrawn from chronic and abusive levels of drug abuse, while group 2 Ss were non-drug users who received acute toxic dosages. Several algorithms were developed to handle the large amount of data to be processed via computer. The spectral analysis algorithm was extensively evaluated, and a special algorithm was applied to EEG amplitude distribution for artifact detection prior to spectral analysis. Power spectra of 30 sec EEG epochs were computed for the entire night and plotted in a compressed spectral array form. The spectrum of each epoch was further decomposed in seven frequency bands, followed by more detailed analyses of each band. Plots for the percentage of power in the delta band during the night clearly showed drug effects on delta-rhythm. Plots for the mean frequency coefficients during the night illustrated quantitatively the manner in which dominant EEG frequencies were shifted as a function of time. The test for Gaussian distribution of the EEG was demonstrated as a drug related parameter. The system required 45 minutes to process an entire night of sleep EEG, which was considerably faster than the time required by a human scorer. (Journal abstract modified)

002869 Parkes, John David. University Department of Neurology, Institute of Psychiatry, London, England **Amphetamines and alertness.** In: Guilleminault, C., Narcolepsy: proceedings. New York, Spectrum, 1976. 707 p. (p. 643-658).

In a paper given at the First International Symposium on Narcolepsy, Montpellier, France, July 1975, the effects of amphetamines on alertness were discussed in terms of neuropharmacology, metabolism, monoamines and sleep, amphetamines and sleep, mode of action in narcolepsy, stereospecificity, related compounds, pharmacodynamics, drug interactions, and drug treatment of narcolepsy. Synthetic amphetamine is a central nervous system stimulant which intravenously causes behavioral and electrical arousal from narcoleptic drowsiness or sleep; prevents sleep and causes euphoria in normal subjects; and increases concentration in fatigued subjects. Amphetamine also causes an increase in body temperature, reduction in appetite and weight, and peripheral effects on blood pressure, pulse rate, bladder sphincter, and tension in skeletal muscle. Therapeutic effects of amphetamines in treatment of narcolepsy have been clinically documented in reducing sleep attacks and cataplexy, although addiction, tolerance, and side-effects (including abnormal behavior) have been reported. 79 references.

002870 Petho, Bertalan. Psychopathological Laboratory, 2nd Clinic for Neurology and Psychiatry, Medical University, Balassa u. 6, H Budapest 1083, Hungary **/Nosotropic effects of psychopharmaceuticals./** Von der nosotropen Wirkung der Psychopharmaka. Psychiatrie, Neurologie und medizinische Psychologie (Leipzig). 28(12):738-746, 1976.

Nosotropic effects of psychopharmaceuticals are reviewed. The spectrum of pharmacogenic pathomorphosis has been found to be dependent also upon the forms of disease, i.e.,the special morbogenic factors. Two opposed types of nosotropy of psychopharmaceuticals, namely, protective and nosogenic nosotropy, are considered in dependence on the pharmacotherapeutic effect produced and the mode of clinical action. Protective and nosogenic nosotropy may be observed to

be active simultaneously and result in characteristic paradoxes of the psychopharmacotherapy of endogenous psychoses. 48 references. (Journal abstract modified)

002871 Rabey, J. M.; Vardi, J.; Ashkenazi, J. J.; Streifler, M. Ichilov Municipal-Government Hospital, Tel Aviv, Israel **L-tryptophan administration in L-dopa-induced hallucinations.** Israel Journal of Medical Sciences (Jerusalem). 12(12):1518-1519, 1976.

A summary of a paper delivered at the 35th meeting of the Israel Physiological and Pharmacological Society of L-tryptophan administration in L-dopa-induced hallucinations is presented. Eight parkinsonian patients who developed visual hallucinations of paranoidal content under L-dopa treatment were given L-tryptophan (50 to 150mg three times a day). L-tryptophan ameliorated the symptomatology in six patients by arresting the visual paranoidal hallucinations or diminishing their frequency and by relieving psychomotor agitation. Three patients reported the experience of pleasurable visual images. The mental disturbances were not affected by L-tryptophan in three patients, but were ameliorated by phenothiazines.

002872 Rapoport, Judith L.; Quinn, Patricia O.; Copeland, Anne P.; Burg, Cheryl. Department of Pediatrics, Georgetown University Hospital, 3800 Reservior Rd., N.W., Washington, DC 20007 **ACTH4-10: cognitive and behavioral effects in hyperactive, learning-disabled children.** Neuropsychobiology (Basel). 2(5/6):291-296, 1976.

The cognitive and behavioral effects of ACTH4-10 on hyperactive, learning disabled children were investigated. ACTH4-10 or placebo was given to a sample of 20 hyperactive, learning disabled children. No significant drug effects were obtained on measures of visual and auditory memory, new learning, impulsivity, attention, perceptual motor skills, anxiety, or behavior during testing. There was a slight increase in pulse rate for drug compared with the placebo group. These findings are in keeping with other recent reports of limited or insignificant cognitive effects in adults of a single dose of this peptide. 18 references. (Author abstract modified)

002873 Saletu, B.; Grunberger, J.; Flener, R.; Linzmayer, L.; Sieroslawski, H. Section of Pharmacopsychiatry, Department of Psychiatry, School of Medicine, University of Vienna, Vienna, Austria **Determination of psychoactivity and cerebral bioavailability of danitracene (WA 335) by quantitative pharmaco-EEG and psychometric investigations.** Current Therapeutic Research. 20(6):810-821, 1976.

In a double-blind study, 10 healthy volunteers received randomized in weekly intervals oral single doses of placebo or danitracene. A 5 minute resting EEG recording and several psychological tests were carried out before as well as 2, 4, 6, and 8 hours after drug administration. The EEG was analyzed offline utilizing digital computer period analysis programs. In contrast to placebo, which did not induce any significant changes, danitracene produced an increase of slow waves, decrease of alpha waves and increase of fast activities, which is typical for thymoleptic drugs. The changes were dose dependent and maximally pronounced 2 hours postdrug. Psychometric tests demonstrated dose dependent decrease in attention and psychomotor activity and a deterioration in mood, which was most pronounced between the second and fourth hour postdrug. There were no changes after placebo, nor were there any changes in blood pressure and pulse after any of the three substances. The findings suggest that: 1) danitracene is CNS effective; 2) its psychoactivity is an antidepressant one; 3) its efficacy is dose dependent; and 4) its effect starts as early as in the second hour postdrug and is maximally pronounced between the second and fourth hour after drug administration, declining thereafter. 19 references. (Author abstract)

002874 Sannita, W. G.; Irwin, P.; Fink, M. Dept. of Psychiatry, School of Medicine, State University of New York, Stony Brook, NY **EEG and task performance after ACTH4-10 in man.** Neuropsychobiology (Basel). 2(5/6):283-290, 1976.

The effects of the heptapeptide ACTH4-10 on electroencephalograms (EEG) memory tests and behavior were examined in 12 normal male volunteers 19 to 29 years old. EEG was recorded for two hours following administration of ACTH4-10 or placebo and was quantified by power spectral density analysis. Drug differences were tested by analyses of variance and covariance. No statistically significant drug effect was found on either EEG or behavioral measures. Of the psychological tests, only the digit span test showed a decrease in number of errors with ACTH4-10. These results are considered to be consistent with previous studies and suggest that intravenous ACTH4-10 has a limited effect on the brain functions tested. 17 references. (Author abstract modified)

002875 Sheldrake, Peter; Cormack, Margaret. Educational Research and Resources Unit, Flinders University of South Australia, Bedford Park 5042, South Australia **Dream recall and the contraceptive pill.** Journal of Nervous and Mental Disease. 163(1):59-60, 1976.

Dream recall ability of women students at Edinburgh University using various types of contraceptive pills was compared to that of nonusers. Data were examined concerning menstrual cycle characteristics, contraceptive pill type, and length of use. The pills were classified in four groups based on their chemical constituents and their estrogenic and progestagenic components. It is suggested that women taking a contraceptive pill are more likely to recall dreaming, and that it is the progestagenic component that is the more active one. However, the data collected do not exclude the possibility that the differences observed are the consequence of other psychological variables, and further research is recommended. 3 references. (Journal abstract modified)

002876 Shopsin, Baron; Kline, Nathan S. Unit for the Study of Affective Disorders, Neuropsychopharmacology Research Unit, NYU Medical Center, New York, NY **MAO inhibitors: potential for drug abuse. (Unpublished paper).** Bethesda, MD, NIMH, 1976. 24 p.

Three cases in which the use of MAO inhibitors was attended with tolerance to the stimulant energizing amphetamine like effect and progressive dose buildup (i.e. "abuse") are presented. The use of the drugs despite the high dosages ingested was accompanied by little or no untoward side-effects even when taken in conjunction with other drugs and foods known to potentially produce delirious synergism. The present data converge with other known clinical and pharmacological findings to suggest that both the MAO inhibitors and amphetamines share common properties including: 1) the induction of euphoriant/stimulating and psychotomimetic effects in certain individuals; 2) both increase, albeit by different mechanisms, the amount of functionally available neurotransmitter (catecholamines and indolamines) at the receptor site; and 3) both classes of drugs can be clinically associated with dependance/tolerance. 33 references. (Author abstract)

002877 Simpson, Dale McClure. Johns Hopkins University, Baltimore, MD **Behavioral effects of repeated psychoactive drug administration. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-22948 HC$15.00 MF$8.50 93 p.

The behavioral effects of repeated psychoactive drug administration were examined, suggesting a new definition for behavioral dependence which is analogous to current definitions of physical dependence. Behavioral dependence was defined in terms of a behavioral withdrawal syndrome which occurs upon termination of drug injections. The possibility of behavioral dependence was then examined for four psychoactive drugs (a stimulant, a tricyclic antidepressant, a monamine oxidase inhibitor, and a phenothiazine). By measuring rates of electrical self-stimulation of the brain in rats, all drugs by the tricyclic antidepressant were shown to produce a characteristic behavioral withdrawal syndrome. This syndrome differed between drugs and was opposite in nature to the acute effects of the relevant drug. The theoretical implications of both behavioral tolerance and dependence were discussed in terms of homeostatic mechanisms regulating a drug's influence on behavior. (Journal abstract modified)

002878 Sinn, Martin; Schiffter, Roland. Department of Neurology, Freie Universitat Berlin, Klinikum Steglitz, D-1000 Berlin, Germany **Propranolol in benign essential tremor.** In: Carlsson, C., Neuro-psychiatric effects of adrenergic beta-receptor. Munich, Urban & Schwarzenburg, 1976. 120 p. (p. 74).

In a paper presented at a symposium on neuropsychiatric effects of adrenergic beta-receptor blocking agents held at Copenhahagen, October 1975, the results of a controlled clinical test of propranolol in the treatment of essential tremor were reported. Sixteen persons underwent a regimen of 40mg per day of propranolol for 1 week, 80mg per day during the second week, placebo during the third week, and 80mg per day of propranolol during the fourth; some patients progressed to a fifth week at 120mg per day. Twelve of the subjects completed the trial. Of these, four rated the effects of propranolol as excellent, seven as good, and one subject reported no effect. Of six patients who subsequently took 120mg propranolol per day, two showed further progress. Ten patients reported aggravation of tremor after the administration of placebo. Essential tremor was found to be significantly reduced under propranolol treatment at a dosage of 80mg per day. Neither the dosage of 40mg propranolol per day nor placebo evidenced significant reduction of benign essential tremor.

002879 Sitaram, N.; Mendelson, W. B.; Dawson, S.; Wyatt, R. J.; Gillin, J. C. Adult Psychiatry Branch, NIMH, Bethesda, MD 20014 **Time-dependent effects of physostigmine on normal human sleep and arousal. (Unpublished paper).** Rockville, MD, NIMH, 1976.

The effects on sleep and arousal of physostigmine infusions administered 5 min and 35 min after onset of sleep, at the onset of rapid eye movement (REM) sleep, and 5 min and 25 min after the end of REM sleep were investigated. Physostigmine induced REM when given 5 min after sleep onset but the drug induced REM more readily when given 35 min after sleep onset. Infusions at REM onset, 5 min after the end of REM, and 25 min after REM produced arousal. A lower dose of physostigmine given 25 min after REM, induced REM sleep without awakening. It is suggested that cholinergic mechanisms are involved in initiating REM sleep and arousal. 1 reference. (Author abstract modified)

002880 Staak, M.; Gottwald, K.; Mallach, H. J.; Schubring, G. Nagelestrasse 5, D-74 Tubingen, Germany **/Pharmacopsychological examinations concerning interactions of alcohol and oxazepam with regard to response behavior./** Pharmakopsychologische Untersuchungen uber Wechselwirkungen zwischen Alkohol und Oxazepam im Hinblick auf das Reaktionsverhalten. International Journal of Clinical Pharmacology and Biopharmacy (Munchen). 14(1):48-65, 1976.

The interactions between oxazepam and ethanol were investigated in a pharmacopsychological study in 14 Ss and the results are reported. Psychomotoric responses showed a tendency towards motoric instability under ethanol, whereas in the placebo experiment a relatively constant level of efficiency was maintained. In the oxazepam experiment a slowing of the psychomotoric functions was observed. The experiments showed a decrease in efficiency during continuous exercise, a delayed response to optic and acoustic stimuli, and a retardation of the entire behavioral pattern under the influence of ethanol and oxazepam. The results indicate the existence of marked interactions between ethanol and oxazepam. 24 references. (Author abstract modified)

002881 Weiss, Bernard; Laties, Victor G. University of Rochester School of Medicine and Dentistry, Rochester, NY **Behavioral pharmacology: the current status.** New York, Plenum, 1976. 301 p. $22.50.

A series of essays dealing with environmental, neurochemical, and toxicological aspects of drug self-administration, and reinforcement contingencies of drug response is presented. Part I covers environmental influences of drug use, behavioral factors of dependence, behavioral functions of narcotic antagonists, experimental models for drug self-administration modification, and methodological developments in alcohol abuse research. In Part II, the interactions of behavioral and neurochemical processes and serotonergic and cholinergic mechanisms in primates, including man, are examined. Part III contains an overview of behavioral toxicology as a discipline, and deals with the effects of amphetamine, mercury and methylmercury on behavior and psychosocial evaluation of toxicity on sensory systems. In the final section, contingencies of reinforcement as determinants of drug response, including schedule controlled behaviors, punished responding, the role of discriminative stimuli, and extrapolations of reinforcement schedules from animals to humans, are discussed.

002882 Zinberg, Norman E. Harvard Medical School, Cambridge, MA 02138 **The war over marijuana.** Psychology Today. 10(7):44-47, 51-52, 102, 104, 106, 1976.

Major research findings on marijuana are summarized in regard to amotivational syndrome, chromosome damage (birth defects), brain damage, psychosis, the steppingstone to heroin theory, interference with the immune response, impairment of sexual activity, incitement to crime, and general health hazards. Since it seems that scientific data do not determine society's responses to the marijuana question, media responses to some of the findings are also considered. It is noted that as much is known about marijuana as about any drug, and it is concluded that marijuana is a remarkably innocuous substance. There are, however, areas of concern: marijuana is an intoxicant and drawing any hot substance into the lungs is not beneficial. It is argued that adolescents under 18 should not use intoxicants of any kind. Only long-term epidemiological surveys can show definitely whether the claims of impairment in sexual drive, lack of resistance to disease, behavioral performance, and birth defects have any validity.

15 TOXICOLOGY AND SIDE EFFECTS

002883 Baldessarini, Ross J.; Tarsy, Daniel. Department of Psychiatry, Harvard Medical School, Neuropharmacology Laboratories, Massachusetts General Hospital, Boston, MA 02114 **Mechanisms underlying tardive dyskinesia.** In: Yahr, M., The basal ganglia. Vol. 55. New York, Raven Press, 1976. 474 p. (p. 433-446).

In a paper presented at the 55th meeting of the Association for Research in Nervous and Mental Disease, mechanisms underlying tardive dyskinesia, including the role of long-term neuroleptic drug therapy and a pathophysiologic state of relative dopaminergic overactivity in the extrapyramidal system were examined. The toxic role of neuroleptics is seen as overemphasized in the literature at the expense of closely examining the physiological and behavioral evidence of a reciprocal functional relationship between dopaminergic and cholinergic mechanisms in the basal ganglia. One explanation of the apparent increase in dopamine activity in tardive dyskinesia may be its increased availability through the well known increase of dopamine turnover in response to neuroleptics, while another may be the development of denervation or disuse supersensitivity of dopamine receptors. The possibility of changes in neuronal systems mediated by other probable CNS synaptic neurotransmitters should also be further investigated, since the disorder could represent toxic or destructive effects on striatal interneurons on which dopamine usually exerts an inhibitory effect, and which in turn may have a feedback influence on nigrostriatal dopamine neurons. Such interneurons may use acetylcholine or gamma-aminobutyric acid. An important experimental test of the drug etiology theory of the disorder would be to reproduce in laboratory animals the neurologic phenomena that occur after prolonged administration of neuroleptics. In the absence of such research, an open-minded attitude toward the disorder is appropriate. 144 references.

002884 Baldessarini, Ross J.; Lipinski, Joseph F. Department of Psychiatry, Harvard Medical School, Boston, MA 02115 **Toxicity and side effects of antipsychotic, antimanic, and antidepressant medications.** Psychiatric Annals. 6(10):52,53,57-59,62-64,67,68, 1976.

The agents currently used in psychiatry have been exposed to unusually thorough and rigorous development and testing to demonstrate their efficacy and safety. Despite the record of therapeutic success and relative safety of these agents, a number of untoward effects remain. Notable are the neuroleptic side effects of virtually all currently available antipsychotic agents. It is concluded that there have been few fundamentally new developments in psychiatric chemotherapy since the late 1950s, and during the past decade the rate of introduction of new agents has diminished greatly. 17 references. (Author abstract modified)

002885 Bertolini, R. Istituti Ospedalieri Neuropsichiatrici S. Lazzaro, Reggio Emilia, Italy **/Therapeutic efficacy of propranolol against tremors and other extrapyramidal effects caused by parkinsonigenic psychotropic drugs./** Efficacia terapeutica del propranololo contro i tremori e contro gli altri effetti extrapiramidali indotti dagli psicofarmaci parkinsonigeni. Rivista Sperimentale di Freniatria (Reggio Emilia). 100(5):1191-1210, 1976.

A study was made of the efficacy of propranolol in treatment of parkinsonian symptoms caused by psychopharmacotherapy. Schizophrenic and psychotic patients 19 to 70-years-old were divided into a group of 20 and a group of 10. The first group received both neuroleptic therapy and propranolol to prevent parkinsonism, and the second group, already showing parkinsonism, received propranolol in place of the promazine derivative antiparkinsonian drugs they had been receiving, such as sulpiride, lithium, fluphenazine, and clothiapine. After 1 month, results showed propranolol was well tolerated by 90% of the 30 patients and no neuroleptic side-effects appeared. Propranolol, like all other antiparkinsonian drugs, has only temporary action, but was especially effective against parkinsonian tremor. 59 references.

002886 Boldyrev, A. I.; Vayntrub, M. Ya. Moskovskiy nauchno-issledovatel'skiy institut psihkiatrii, Ministerstva zdravookhraneniya RSFSR, Moscow, USSR **/Clinical characteristics of psychopathological changes produced by pharmacological antiepileptic therapy./** Klinicheskaya kharakteristika psikhopatologicheskikh izmeneniy, vyzvannykh medikamentoznoy protivoepilepticheskoy terapiyey. Zhurnal Nevropatologii i Psikhiatrii Imeni S. S. Korsakova (Moskva). 76(8):1224-1227, 1976.

A total of 48 cases are reported in which antiepileptic drugs induced psychopathological changes. The drugs involved phenobarbital alone and phenobarbital in combination with bromural, hexamidine (Mysoline), diphenylhydantoin, phinlepsin, benzonol, chlordiazepoxide, and diazepam. The epileptics included patients with grand mal, petit mal, and psychomotor epilepsy. The 18 males and 30 females ranged in age from 17 to 53 years. The types of psychopathology seen following treatment with antiepileptic drugs ranged from dysphoria and dysthymia to derealization, depersonalization, deja vu, oneiroid states, and hallucinations. 9 references.

002887 Bourgeois, M.; Bouey, P. U.E.R. de Psychiatrie (Universite Bordeaux II), 121, rue de la Bechade (centre Carneire), F-33076 Bordeaux, France **/Antagonism between antiparkinsonian drugs and neuroleptics: several experiences of withdrawal, including a personal experience. Part 2./** L'antagonisme entre correcteurs anti-parkinsoniens et neuroleptiques. A propos de diverses experiences de sevrage dont une personnelle (2e partie). Annales Medico-Psychologiques (Paris). 2(4):699-708, 1976.

A paper presented at the October 1976 session of the Societe Medico-Psychologique reported on pharmacological antagonism between antiparkinsonian drugs and neuroleptics, revealed by sampling of neuroleptics blood levels and by experience in withdrawal of corrector agents, in which 35 chronic patients were taken off correctors. Twelve patients had to resume correctors for neurological and/or psychiatric reasons: acute dyskinetic crisis (1 case), Parkinson syndrome: akinetic hypertension plus tremor (5 cases), delirious reactivation plus akinetic depression (2 cases), akinetic depression (1 case), and discomfort of patient asking to resume the corrector (3 cases). In many cases of extrapyramidal syndrome, a decrease of neuroleptic rather than an increase seems to be advisable, because the correctors diminish the neuroleptics up to 44%. These correctors have a psychotropic action which was not known until recently, because they were recommended only on the basis of the extrapyramidal syndrome of neuroleptics, whose elements they correct only partially. Because of early antagonism between neuroleptics and correctors (probably in the alimentary canal) it is recommended that the two drugs be given separately. 7 references.

002888 Bourgeois, M.; Mazaux, J.-M.; Imbert, D.; Daubech, M.-J.-P.; Daulouede, J.-P.; Tignol, J. U.E.R. de Psychiatry, Universite Bordeaux II, 121, rue de la Bechade, F-33076 Bor-

deaux, France /**Use of so-called antiparkinson medications in psychiatry.**/ De l'emploi en psychiatrie des medicaments dits correcteurs antiparkinsoniens. Annales Medico-Psychologiques (Paris). 2(3):499-510, 1976.

The use of antiparkinson medications in psychiatry was discussed at the 1976 session of the Societe Medico-Psychologique. The four types of extrapyramidal syndrome discussed are: initial akinesia without hypertonia, early paroxysmal excitomotor syndrome (dystonia), akinetohypertonic syndrome (parkinsonism), and hyperkinetohypertonic syndrome (akathisia). There are also tardive dyskinetic or hyperkinetic syndromes. The development of extrapyramidal syndromes depends upon individual predisposition, the type of major tranquilizer used, and the dosage used. The antiparkinson medications are reviewed. They are most effective in hypertonia, less effective in akinesia, slightly effective in akathisia, and without effect in chronic (tardive) dyskinesia. As anticholinergics, the antiparkinson drugs cause a confused state and have an antidepressant effect. They also have been used in treating addicts. 32 references.

002889 Brown, T. C. K. Dept. of Anesthesia, Royal Children's Hospital, Flemington Road, Parkville, Victoria 3052, Australia **Sodium bicarbonate treatment for tricyclic antidepressant arrhythmias in children.** Medical Journal of Australia (Glebe). 2(10):380-382, 1976.

The use of sodium bicarbonate in the treatment of arrhythmias in the intensive care unit at the Royal Children's Hospital, Melbourne, Australia, is outlined, and findings on the treatment of tricyclic antidepressant arrhythmias are summarized. Sodium bicarbonate was used on 12 children (8 had ingested imipramine, 2 had ingested amitriptyline, and 2 had ingested nortriptyline): the arrhythmias varied and included multifocal ventricular extrasystoles, runs of ventricular tachycardia, and varying degrees of heart block. There have been no deaths since the use of sodium bicarbonate has become routine in the treatment of tricyclic antidepressant arrhythmias. Clinical data are presented to support the finding that sodium bicarbonate is the most clinically effective method of treatment of these arrhythmias in children. 14 references.

002890 Burckhardt, D.; Fleischhauer, H.-J.; Muller, Verena; Neubauer, H. W. Medizinische Universitatspoliklinik, Hebelstr. 1, CH-4056 Basel, Switzerland /**The effect of tricyclic and tetracyclic antidepressants on the heart and circulation.**/ Beitrag zur Wirkung tri- und tetrazyklischer Antidepressiva auf Herz und Kreislauf. Schweizerische Medizinische Wochenschrift (Basel). 106(52):1896-1903, 1976.

The effects of tricyclic and tetracyclic antidepressants on cardiovascular function were investigated. Preparations included trimipramine, amitriptyline, maprotiline, mianserin, and imipramine. EKG, pulse frequency, and blood pressure of 47 patients were recorded before, during, and after medication. All had been on antidepressants for at least 3 weeks; final recordings were made 4 weeks after withdrawal of drugs. Nineteen other patients whose drug intake could not be curtailed were tested an average of 13 months after inception. No significant arrhythmias were noted. Prolangation of PR interval, extension of QRS, prolongation of QTC time and T-wave flattening proved to be reversible. No differences were noted in the effect of tricyclic and tetracyclic compounds. Caution is nevertheless indicated during the first 3 weeks of drug administration. It is recommended that patients be monitored for clinical signs of cardiac insufficiency, arrhythmia, and intolerance. The study did not find age, drug composition, or duration of intake to be decisive. 31 references.

002891 Chadwick, D.; Reynolds, E. H.; Marsden, C. D. University Department of Neurology, King's College Hospital Medical School, London, England **Anticonvulsant-induced dyskinesias: a comparison with dyskinesias induced by neuroleptics.** Journal of Neurology, Neurosurgery, and Psychiatry (London). 39(12):1210-1218, 1976.

Anticonvulsant induced dyskinesias are compared with those induced by neuroleptics and case histories of both kinds are examined. Anticonvulsants cause dyskinesias more commonly than has been appreciated. Diphenylhydantoin (DPH), carbamazepine, primidone, and phenobarbitone may cause asterixis. DPH, but not other anticonvulsants, may cause orofacial dyskinesias, limb chorea, and dystonia in intoxicated patients. These dyskinesias are similar to those caused by neuroleptic drugs and may be related to dopamine antagonistic properties possessed by DPH. 31 references. (Author abstract)

002892 Colonna, L. Hopital Psychiatrique, 76-Sotteville-les-Rouen, France /**Paradoxic effects of neuroleptics?**/ Effets paradoxaux des neuroleptiques? Encephale (Paris). 2(3):197-200, 1976.

Two cases of agitation and hallucinations resulting from high doses of haloperidol were reported at the 10es Journees d'Information Psychiatrique, Marseilles, 1976. A 46-year-old female received 300 drops/day Moditen, 250 drops/day Nozinan, and 100mg/day amitriptyline. Because of a persistent delirium and hallucinatory syndrome, 90 drops/day haloperidol was substituted for the above and was progressively increased to a dose of 600 drops/day, which was maintained for 7 months. During this period, the patient's clinical state aggravated and she developed anxiety, agitation, insomnia, and depression. The dose of haloperidol was reduced, then discontinued, and Nozinan, 200 drops/day, was administered and subsequently reduced to 80 drops/day. The patient's condition improved and the agitation, hallucinations, and depression disappeared. The other patient was a 39-year-old male who was receiving 60 drops/day haloperidol and 50 drops/day Nozinan. He also had delirium and hallucinatory syndrome. Nozinan was eventually discontinued and haloperidol increased to a dose of 600 drops/day which caused aggravation of anxiety, agitation, and hallucinations, and appearance of depression. When the haloperidol dose was reduced to 100 drops/day, hallucinations and anxiety decreased, sleep improved, and normal mood returned.

002893 Engel, R. R.; Fischer, J.; Greil, W. Psychiatrische Klinik der Universitat Munchen, Nussbaumstrasse 7, D-8000 Munich 2, Germany /**Direct quantitative measurement of tremor: initial results of a new measuring procedure in patients under lithium treatment.**/ Direkte quantitative Tremormessung: Erste Ergebnisse eines neuen Messverfahrens bei Patienten unter Lithium-Behandlung. Arzneimittel-Forschung (Aulendorf). 26(6):1126-1128, 1976.

A piezoelectric miniature receiver for direct measurement of tremor is described. The device is 3.3x 3.5x 7.6mm in size and weighs 0.25g. In 34 patients undergoing prolonged lithium therapy the instrument was put on the forefinger of the right hand, and tremor was measured for 10 sec periods as the fingers were held outstretched and as a pencil was held. Test/retest correlations varied from 0.75 to 0.94, with the interval between tests varying from 30 min to 4 days. Some of the usual indirect methods for the assessment of tremor showed very low correlations with the true tremor amplitude and were therefore of limited usefulness. 1 reference.

002894 Floyd, John B., Jr.; Murphy, C. Michael. no address **Hallucinations following withdrawal of valium.** Journal of the Kentucky Medical Association. 74(11):549-550, 1976.

Five cases of withdrawal from valium were observed over a 3 year period. Pattern was similar in each case, the patient becoming confused, disoriented, and suffering personality change within 72 to 144 hours following hospitalization. Background studies revealed that all had been consuming 20 to 40mgm of valium per day over a period of years. The magnitude of the problem can be realized by the 1972 pharmaceutical report of 144,000,000 prescriptions for sedatives, one third of these being for valium. 5 references.

002895 Fukatsu, Ryo; Saito, Yoshiro; Miyagishi, Tsutomu; Takahata, Naohiko; Suwa, Nozomu. Department of Neuropsychiatry, Hokkaido University, Hokkaido, Japan **Psychotic symptoms resulting from steroid use -- especially light consciousness impairments.** Psychiatria et Neurologia Japonica (Tokyo). 78(8):581, 1976.

In a paper read at the 48th Hokkaido Psychoneurological Symposium held in December 1975 at Sapporo, Japan, three cases who exhibited psychotic symptoms (thought to be related to Durchgang's syndrome) resulting from administration of steroid drugs are reported. Common symptoms of the three included: hyperactivity, periods of euphoria and depression, withdrawal, personality change, tremors, delirium, hallucinations, and delusions. Brainwave measurements showed distortion in slow waves. All symptoms disappeared upon withdrawal from the steroids, and they were thought to represent a multicausal consciousness impairment.

002896 Ganz, Varda Peller; Volkmar, Fred. Department of Counseling and Psychological Services, Cowell Student Health Center, Stanford University, Stanford, CA 94305 **Adverse reactions to marihuana use among college students.** Journal of the American College Health Association. 25(2):93-96, 1976.

Case histories of five college students with adverse reactions to marihuana use ranging from depression and anxiety neurosis to hallucination recurrence are presented. All patients were administered psychotropic drugs to counter immediate symptoms. Cessation of marihuana use resulted in alleviation of the symptoms, and psychotherapy was undertaken to treat underlying psychological problems. Although most chronic marihuana users report no adverse effects, a small population has adverse reactions and discontinuance of marihuana use is difficult for them. In the five cases presented, the patients had been using marihuana to reduce anxiety and stress, and although aware of the adverse effects, periodically resumed use with a concomitant resumption of symptoms. 16 references.

002897 Gifford, Sanford; Murawski, Benjamin J.; Kline, Nathan S.; Sachar, Edward J. Department of Psychiatry, Peter Bent Brigham Hospital, 721 Huntington Ave., Roxbury MA 02115 **An unusual adverse reaction to self-medication with prednisone: an irrational crime during a fugue-state.** International Journal of Psychiatry in Medicine. 7(2):97-122, 1976.

The case study is of a 41-year-old asthmatic man is presented, who during 5 years of self-medication with prednisone experienced: 1) periods of euphoria, psychomotor hyperactivity and poor judgment; 2) a period of depression and anxiety during temporary steroid withdrawal; and 3) with resumption of prednisone, episodes of grandiosity and bizarre fugue like behavior, with adoption of a second identity and culminating in an irrational crime. Steroids were then withdrawn, and the patient resumed his premorbid personality, but had amnesia for much of his previous behavior. The literature on hysterical fugues and corticosteroid induced mental disturbance is reviewed. The patient's reactions are analyzed in terms of his premorbid neurotic conflicts, the psychological stresses acting upon him and the effects of prednisone on his central nervous system. 34 references.

002898 Girard, J.; Girard, Josette. C. H. U., Clermont-Ferrand, France **/Surmontil and muco-cutaneous pigmentation./** Surmontil et pigmentation cutaneo-muqueuse. Annales Medico-Psychologiques (Paris). 1(4):580, 1976.

A case of mucous and cutaneous pigmentation following 9 years of treatment with trimipramine (Surmontil) was reported at the November 22, 1975 meeting of the Societe Regionale de Neuro-Psychiatrie et de Psychologie Clinique de Clermont-Ferrand. Confluent spots of a brownish color were present on the interior of the lips and cheeks. Increase in pigmentation was halted by cessation of the trimipramine, but the pigmentation regressed only slightly.

002899 Glover, Dianne; Gerety, Meghan; Bromberg, Shirley; Fullam, Susan; DiVasto, Peter; Kaufman, Arthur. no address **Diethylstilbestrol in the treatment of rape victims.** Western Journal of Medicine. 125(4):331-334, 1976.

The use of diethylstilbestrol (DES) as a "morning after pill" for rape victims is assessed, the risks involved with DES described, and guidelines for its continued use proposed. Of 150 consecutive rape victims treated at a university medical center, 63 (42%) received prescriptions for DES. Of the 55 (87%) on whom followup was obtained, in 40 (73%) there were substantial side-effects -- nausea, vomiting, or both. At least six (11%) did not complete therapy because of these side-effects. The decision to employ this drug must be made after allowing the patient to weigh the risk of pregnancy and abortion against the likelihood of DES side-effects. The physician's role is to offer options. 11 references.

002900 Gold, Donald D., Jr. University of Tennessee, 800 Madison Ave., Memphis, TN 38163 **Antipsychotic agents and serum prolactin levels.** Journal of the American Medical Association. 236(19):2175, 1976.

The possible harmful side-effects of the phenothiazines and certain other neuroleptic drugs are considered. It has been hypothesized that the possible increased incidence of breast cancer among hypertensive patients receiving reserpine may be related to increased circulating serum prolactin levels. While reserpines are essentially no longer used in psychiatric treatment, phenothiazines and some other neuroleptic drugs have been clearly demonstrated to increase serum prolactin levels in man. It is thought that if the hypothesized connection between serum prolactin level and breast cancer is correct, it could have profound ramifications for a large number of psychiatric patients. 1 reference.

002901 Goldstone, Sanford; Lhamon, William T. Edward W. Bourne Behavioral Research Laboratores, 21 Bloomingdale Road, White Plains, NY 10605 **The effects of haloperidol upon temporal information processing by patients with Tourette's syndrome.** Psychopharmacology (Berlin). 50(1):7-10, 1976.

Tourette's syndrome patients treated successfully with haloperidol, untreated patients, and healthy controls were studied with tests of temporal discrimination and measures of transmitted information, shown previously to be sensitive to brain dysfunction, in order to assess the effects of haloperidol

upon temporal information processing by patients. Two psychophysical methods (single stimuli and pair comparison) and fewer (3 stimulus/3 response), or more (5 stimulus/5 response) judgement alternatives were employed among the 22 subjects to sample the effects of different cognitive demands and loads. Untreated patients showed no impairment of temporal processing, while those treated with haloperidol showed significant deficit in amount of transmitted information comparable to prior studies of brain syndromes. These results indicate a toxic potential of haloperidol in a nonpsychotic population. 11 references. (Author abstract modified)

002902 Gossain, Ved V.; Hagen, Garrett A; Sugawara, M. Department of Medicine, B234 Life Sciences I. Michigan State University, East Lansing, MI 48824 **Drug-induced hyponatraemia in psychogenic polydipsia.** Postgraduate Medical Journal (Oxford). 52(613):720-722, 1976.

Case reports of two patients with psychogenic polydipsia who developed hyponatremia, one in association with administration of hydrochlorothiazide and the other in assocation with tolbutamide, are presented. These effects may be the result of enhancement of antidiuretic hormone (ADH) already present or stimulation of ADH release. It is suggested that increased fluid intake in patients with polydipsia may make them more susceptible to the development of hyponatremia from thiazide or sulphonylurea compounds, and greater caution in the administration of these drugs to such patients is recommended. 12 references. (Author abstract modified)

002903 Granacher, Robert P.; Baldessarini, Ross J.; Messner, Edward. Intensive Treatment Service, Eastern State Hospital, Lexington, KY **Physostigmine treatment of delirium induced by anticholinergics.** American Family Physician. 13(5):99-103, 1976.

The central anticholinergic toxicity syndrome, which may be induced by a variety of medications in use in family practice, and which is characterized by delirium and disordered behavior, is described, and its treatment with physostigmine is recommended. Toxic delirium, which may resemble an acute psychosis, can occur as an adverse drug reaction to properly prescribed anticholinergic medication and to recommended doses of many patent medicines. More frequently it is due to overdosage. The key to diagnosis is the presence of peripheral signs of parasympathetic blockade. Delirium induced by anticholinergic drugs can be treated rapidly and effectively with physostigmine salicylate. (Author abstract)

002904 Grof, P.; MacCrimmon, D.; Saxena, B.; Daigle, L.; Prior, M. Dept. of Research Hamilton Psychiatric Hospital, Hamilton, Ontario, Canada **Bioavailability and side effects of different lithium carbonate products.** Neuropsychobiology (Basel). 2(5/6):313-323, 1976.

The bioavailability and the side-effects of three different lithium carbonate products were compared. Among the three lithium preparations tested, no significant difference was found in the bioavailability, as expressed in serum and erythrocyte lithium concentrations and urinary lithium output. The side-effect reports, however, varied significantly among the types of lithium under study. The slower the absorption of a particular preparation, the fewer the side-effects. The results of this study suggest that preference be given to lithium preparations with slow release properties particularly in side-effect prone subjects. 13 refefences. (Author abstract modified)

002905 Halbreich, Uriel; Assael, Marcel. Psychiatric Department, Kaplan Hospital, Jerusalem, Israel **'Clubbing' -- a side-effect of long-term phenothiazines treatment.** Confinia Psychiatrica -- Borderlands of Psychiatry (Basel). 19(2):96-98, 1976.

The symptom of clubbed fingers was investigated as a possible side-effect of long-term treatment with phenothiazines. A paranoid schizophrenic patient received continuous maintenance treatment with phenothiazines for 5 years. Eight weeks after switching to fluphenazine enanthate injections intramuscularly, clubbed fingers occurred. The results of thorough medical examinations were within normal limits; consequently, the phenothiazine treatment was presumed to be the cause of clubbing. It is suggested that anoxia of the distal tissue gives rise to clubbing due to arterial hypotension, slowing down of the blood flow, and viscosity of the blood. (Journal abstract modified)

002906 Hallstrom, C.; Gifford, L. Maudsley Hospital, Denmark Hill, London SE5 8AZ, England **Antidepressant blood levels in acute overdose.** Postgraduate Medical Journal (Oxford). 52(613):687-688, 1976.

To determine if there were any possible relationships between plasma antidepressant levels and physiological measures, plasma antidepressant levels and clinical condition were measured sequentially for at least 24 hr in eight patients who presented with acute antidepressant overdosage. There was no evidence to suggest that a knowledge of the drug plasma levels had anything to offer in the management of a patient whose overdose included a tricylic antidepressant. 4 references. (Author abstract)

002907 Johnson, N. McI.; Copeland, G. P.; Clarke, S. W. Royal Free Hospital, London NW3 2QG, England **Severe neutropenia urticaria with antidepressant therapy.** Lancet (London). No. 1779:1357, 1976.

A case of severe neutropenia probably associated with maprotiline hydrochloride (Ludiomil), a tetracyclic antidepressant, is reported. The patient, a 39-year-old woman with marital problems and reactive depression, complained of malaise, nausea, and headaches. Imipramine 10mg t.i.d. was prescribed. Since no symptomatic improvement occurred after 3 weeks, imipramine was stopped and maprotiline 75mg at night was prescribed. Three days later the patient complained of maculopapular rash with areas of urticaria. The drug was stopped and the rash improved with chlorpheniramine and calamine lotion. However, 4 days later the patient complained of a sore throat with buccal ulceration, headache, fever, aching of the arms and legs and cervical lymphadenopathy. The patient was hospitalized and after further studies and medication she recovered within 3 weeks. It is concluded that the patient's severe neutropenia was caused by the maprotiline hydrochloride.

002908 Kaji, Shizuo. Department of Psychiatry, Niigata University, School of Medicine, Niigata, Japan **Influence of psychotropic drug treatment upon pentamethylenetetrazol threshold in non-epileptic psychotic patients.** Clinical Psychiatry (Tokyo). 18(1):59-66, 1976.

Pentetrazol threshold levels were measured in nonepileptic patients who were taking psychotropic drugs (23 taking reserpine (RES), 9 taking chlorpromazine (CPZ), 2 taking both RES and CPZ, and one patient taking RES and perphenazine). Of the 35 subjects, 13 had levels of pentetrazol below 7.9mg/kg, 7 had low levels of below 5.9mg/kg, and the remaining 22 had

levels above 8mg/kg. There were some variations in these threshold levels upon further measurements. It was thought that the appearance of seizures in some patients who are taking psychotropic drugs have "latent epileptic tendencies" which could be caused by the existence and functions of some neural damage. 34 references.

002909 Kaneya, Shun; Kaneya, Akira; Wagatsuma, Shunsuke. Department of Psychiatry, Ohta General Hospital, Ohta, Japan **Two cases of serious side-effects during pharmacotherapy.** Psychiatria et Neurologia Japonica (Tokyo). 78(8):570-571, 1976.

In a paper presented at the 30th Northern Japan Psychoneurological Symposium held in September 1975 in Akita, Japan, two cases in which long-term use of chlorpromazine was thought to be responsible for serious side-effects are described. In one case, a 40-year-old schizophrenic who had been taking chlorpromazine (in both cases dosage was between 100 and 150mg) for 12 years quickly developed profuse sweating and swelling of the abdomen which produced shock and eventually death. In the second case, another 40-year-old schizophrenic who had been on chlorpromazine and other psychotropic drugs suddenly developed impaired consciousness, fever, vomiting, and lapsed into a coma. He recovered after 6 days. Autopsy of the first case indicated paralysis due to psychotropic drugs. Debate of the second case also indicated a probable cause of psychotropic drug usage and addiction.

002910 Klawans, Harold L. Division of Neurology, Michael Reese Hospital and Medical Center, Chicago, IL 60616 **Therapeutic approaches in neuroleptic-induced tardive dyskinesias.** In: Yahr, M., The basal ganglia. Vol. 55. New York, Raven Press, 1976. 474 p. (p. 447-457).

In a paper presented at the 55th meeting of the Association for Research in Nervous and Mental Disease, therapeutic approaches to neuroleptic induced tardive dyskinesia, an iatrogenic disorder caused by exposure to these pharmacological agents, were described. The role of dopamine in these choreatic states must be understood, since both tardive dyskinesia and levodopa induced dyskinesia may be conceptualized as abnormal hyperactive responses of striatal dopamine receptors to dopamine. Steps in preventing development of the disorder include: 1) decrease the number of patients at-risk by restricting use of neuroleptics; 2) avoid prolonged use of anticholinergic agents as an adjunct treatment, since dopamine related, amphetamine induced, stereotyped behavior in animals suggests that they may increase severity of dyskinesia in patients prone to this type of movement disorder and increase its incidence by altering the threshold for appearance of the characteristic movements; 3) keep neuroleptic daily doses as low as possible, use frequent drug holidays, and limit duration of treatment; and 4) emphasize early diagnosis and intervention. The disorder is not always irreversible, and therapy is based on the use of agents such as reserpine that decrease dopamine activity at dopamine receptors, along with discontinuation of anticholinergic agents. Recent findings also suggest that different dopamine receptor systems are involved in tardive dyskinesia and schizophrenia, and indicate that the disorder is not inevitable. Drugs such as clozapine, which is capable of blocking mesolimbic dopamine receptors involved in schizophrenia and has no effect on the striatal dopaminergic systems involved in tardive dyskinesia, are therefore recommended. 49 references.

002911 Kobayashi, Ronald M. Neurology Service, Veterans Administration Hospital, 3350 La Jolla Village Drive, San Diego, CA 92161 **Orofacial dyskinesia -- clinical features, mechanisms and drug therapy.** Western Journal of Medicine. 125(4):277-288, 1976.

The clinical features, mechanisms, and drug therapy of orofacial or tardive dyskinesias, involuntary repetitive movements of the mouth and face, are discussed. In most cases, they occur in older psychotic patients who are in institutions and in whom long-term treatment with antipsychotic drugs of the phenothiazine and butyrophenone groups is being carried out. These dyskinesias are frequent in occurrence and characteristically are irreversible. Several biochemical mechanisms have been proposed as causes, including hypersensitivity or partially deneverated brain dopamine receptors and low affinity of the offending drugs for brain muscarinic cholinergic receptors. Clinical therapy has been attempted primarily with drugs that antagonize dopamine receptors or deplete brain dopamine. The benefits of drug treatment have been variable and lack of consistent improvement has been discouraging. Early recognition of dyskinesia should be attempted, and the dose reduced or the drug omitted at the first sign. 102 references. (Author abstract modified)

002912 Korczyn, A. D.; Goldberg, G. J. Department of Physiology and Pharmacology, Sackler School of Medicine, Tel-Aviv University, Ramat-Aviv, Israel **Extrapyramidal effects of neuroleptics.** Journal of Neurology, Neurosurgery, and Psychiatry (London). 39(9):866-869, 1976.

Neurologic examinations of 66 psychiatric patients who took major tranquilizers for periods of 4 to 16 years were conducted to determine toxic effects of chronic administration. The frequency of signs of Parkinsonism and the effects of orphenadrine were studied in a double-blind crossover method. Of the patients in the study, 61% showed signs of Parkinsonism. Female patients and those with organic brain pathology more frequently exhibited Parkinsonism. No correlation was found between duration of treatment and extrapyramidal effects. Of the 40 patients who developed Parkinsonism, 25 responded favorably to orphenadrine, while 6 had more marked extrapyramidal manifestations on orphenadrine than on placebo. 11 references. (Author abstract modified)

002913 Lutz, Elmar G. 896 Valley Road, Wayne, NJ 07470 **/Extrapyramidal side-effect of certain tranquilizers./** Akathisia. Clinical Medicine. 83(12):14-20, 1976.

The appearance of akathisia, or motor restlessness, both in high dosage administration of certain tranquilizers and in cases of brain disease or dysfunction is discussed. Frequently extrapyramidal side-effects occur after administration of low dosages in certain individuals with a biologic specificity for certain molecular structures, and that the susceptibility to this side-effect is increased when there is brain disease or temporary brain dysfunction. Akathisia caused by the most potent phenothiazines (trifluoperazine or fluphenazine) is considered to be the hardest to control. It is concluded that whenever a patient responds paradoxically to or fails to respond to the administration of a neuroleptic, the possibility of akathisia should be considered and appropriately treated. Usually, removal of the offending drug relieves the problem. Antiparkinsonian agents may speed the reversal of these side-effects.

002914 Makulova, I. D.; Filicheva, A. P. Institut usovershenstvovaniya vrachey im. C. M. Kirova, Leningrad, USSR **/Health status in persons engaged in the production of triftazine./** Sostoyaniye zdorov'ya lits, zanyatykh v proiz-

vodstve triftazina. Gigiyena Truda i Professional'nye Zabolevaniya (Moskva). No. 7:27-30, 1976.

The status of health of 57 workers, up to 40 years old, who had worked 2 to 5 years in the production of triftazine (stelazine) was assessed by medical examination. About 40 percent complained of cephalalgia, vertigo, and pain in the heart region. Vegetative/vascular disorders in combination with neurasthenic syndrome were frequently noted. Hemodynamic oscillographic investigations disclosed a drop in oscillatory index, asymmetry of indicators, and a rise in mean pressure in most workers. Examination of the peripheral blood revealed a drop in hemoglobin, reticulocytes, and thrombocytes, and an increase in leukocytes accompanied by a decrease in lymphocytes and monocytes. These changes increased in intensity with an increase in years worked. It is concluded these medical changes are due to the chronic action of triftazine. 6 references.

002915 Marriott, P. 96 Grattan Street, Carlton, Victoria 3053, Australia **Overuse of synthetic anticholinergic drugs in psychiatry.** Medical Journal of Australia (Glebe). 2(17):663-664, 1976.

In a letter to the editor, the side-effects of anticholinergic drugs which are taken continuously (insomnia, drug dependency, and perhaps tardive dyskinesia), and which should be known by doctors who have patients with chronic psychiatric illnesses who use these antiparkinsonian drugs, are discussed. Nontherapeutic drug interactions include a lowering of plasma chlopromazine levels with benzhexol. With the delay in gastric emptying, due to the anticholinergic properties, the phenothiazines may be broken down into the inactive metabolites and be less clinically effective. Not all the extrapyramidal side-effects of the phenothiazines are modified by the addition of atropine-like drugs (for example, benztropine), nor do they prevent the appearance of such side-effects if given prophylactically. Generally, with the oral forms of phenothiazines, the antiparkinsonian drug can be withdrawn or its dose reduced some 3 to 6 months after side-effects have been controlled. 2 references.

002916 Marsden, C. D. University Department of Neurology, Institute of Psychiatry and King's College Hospital Medical School, London, S.E.5, England **Dystonia: the spectrum of the disease.** In: Yahr, M., The basal ganglia. Vol. 55. New York, Raven Press, 1976. 474 p. (p. 351-367).

In a paper presented at the 55th meeting of the Association for Research in Nervous and Mental Disease, the concept of dystonic muscle contraction and the syndrome of torsion dystonia were examined. Various manifestations of idiopathic torsion dystonia in childhood and adulthood were detailed, along with the concept that various isolated entities in adult life, such as writer's cramp, spasmodic torticollis, blepharospasm, and oromandibular dystonia, are manifestations of adult onset torsion dystonia. Dystonia remains a clinical concept of abnormality of muscle contraction, which, when it causes abnormal movements and postures characteristic of torsion dystonia, assumes the status of a clinical syndrome. Torsion dystonia, the syndrome, may be due to recognizable diseases, identified either by additional clinical features or by distinctive pathological brain changes (symptomatic torsion dystonia). Idiopathic torsion dystonia varies in mode of presentation, extent of progression, and inheritance dependent on age. The spectrum of idiopathic torsion dystonia, or dystonia musculorum deformans, may therefore extend from the child with inherited severe generalized progressive dystonia to the adult with an isolated nonprogressive focal dystonia, such as spasmodic torticollis. It is likely that this spectrum is due not only to the effect of age on the expression of a single etiology, but also to the existence of a number of causes for the condition. 35 references.

002917 Muniz, Carlos E.; Gervais, Robert H. Shands Teaching Hospital and Clinics, University of Florida, Gainesville, FL **Lithium therapy: a brief review.** Rocky Mountain Medical Journal. 73(5):257-260, 1976.

Clinical and therapeutic indications, dosage and toxicity of lithium are briefly reviewed. It is stated that because lithium is a lifetime medication and because of its potential toxicity, pharmacological knowledge of lithium is a necessity for psychiatrists and physicians. Although perhaps the best therapeutic indication for lithium is prophylaxis of episodes of mania and/or depression in bipolar cases, lithium also has been used in schizoaffective disorders and to curb aggression. Lithium is not bound to serum or tissue protein, although toxic symptoms usually correlate with serum levels and are associated mainly with the central nervous system. Lithium toxicity is differentiated from undesirable somatic side-effects without clinical significance. 11 references.

002918 Nakamura, Hiroshi; Mizuno, Takumi; Kawamura, Katsuhiko; Kamino, Tetsuro; Nakaosa, Toyohisa; Matsushima, Eiichi. Osaka-Minami National Hospital, Osaka, Japan **Creative phosphokinase activity and acid-base balance in cerebrospinal fluid after poisoning with hypnotics (ethinamate).** Iryo (Tokyo). 30(2):107-112, 1976.

Enzymatic activities and gas analysis in cerebrospinal fluid (CSF) of a 24-year-old male who attempted suicide by ethinamate poisoning was used to investigate increases in the activities of cerebrospinal fluid enzymes, particularly creative phosphokinase (CPK), which are frequently noted in CNS disorders. Levels of other enzymes in CSF were not elevated, but the activity of CSF-CPK increased markedly to 87 units. pH and HC03 in CSF were decreased to 7.233 and 9.9mEq per liter, respectively, and CSF oxygen tension diminished slightly. On the basis of observations that in almost all cases of cerebrovascular insufficiency (CVI), CPK activity tends to be greater than in normal or control cases of CVI, it is presumed that hypoxia or acidosis might be one of the factors by which the level of CPK in CSF might be elevated. 24 references. (Journal abstract modified)

002919 no author. no address **Glutethimide -- an unsafe alternative to barbiturate hypnotics.** British Medical Journal (London). No. 6023:1424-1425, 1976.

Reports that glutethimide poisoning is an even greater danger to life than comparable barbiturate overdosage are discussed. An American investigation showed the overall mortality from glutethimide and barbiturate poisoning to be 13.9% and 0.7%, respectively, while a Danish study reported corresponding values of 14.1% and 1.8%. Another American study found glutethimide to have the highest mortality of all drug induced comas (17%). Two British studies report mortalities from glutethimide at only 6% and 1.4%. Glutethimide causes as much respiratory depression and hypotension as do barbiturates and more pulmonary edema, cerebral edema, convulsions, and sudden apnea. Glutethimide also induces dependence. Nitrazepam is recommended as a safe hypnotic, since an individual can ingest as much as 60 to 70 tablets without becoming more than drowsy, and a dose of 10mg is effective in providing sleep and is as effective as 200mg butabarbital. If nitrazepam overdose has ever caused death, its frequency has been minute. 13 references.

002920 no author. no address **Cannabis psychosis.** British Medical Journal (London). No. 6044:1092-1093, 1976.

Psychotic reactions associated with the use of cannabis are discussed. Acute psychotoxic reactions described include paranoia, hallucinations, depersonalization, delirium, disorientation and severe panic, and seem to often be dose related. Cannabis psychosis is generally used to describe reactions to long-term use. A review of research into cannabis psychosis is presented; concurrence in these studies of periodicity, short duration, precipitation by increased dose, relapse after resumption of use and tendencies toward violence and restlessness has been found. It has been suggested that heavy and prolonged cannabis use leads to tolerance until a saturation point is reached where further increase leads to decompensation of mental function and resulting psychosis. It is concluded that studies of cannabis psychosis to date have paid too little attention to personality, genetic or environmental factors which may effect the individual's vulnerability, and that it seems unlikely that one drug could cause hysterical reactions, mania, and schizophrenia. While it is possible that cannabis may act as a precipitating factor, more research is needed. 28 references.

002921 Ogura, Chikara; Koga, Itusyuki; Akamatsu, Tetsuo; Kuda, Kenji; Ueta, Hajime; Okuma, Teruo; Shimao, Syuhie; Mihara, Motoyuki; Inoue, Taeko. Department of Neuro-Psychiatry, Tottori University, School of Medicine, Tokyo, Japan **Dermatological findings on neuro-psychiatric patients during psychopharmacotherapy.** Clinical Psychiatry (Tokyo). 18(1):67-76, 1976.

Hospitalized neurotics (N=317) who were taking psychotropic drugs were given a whole body dermatological examination to investigate any relationship between skin abnormalities and the psychotropic drugs. Dermatological abnormalities were found in 94.6%; 31.9% had pigment irregularities, 24.6% had cornification of the skin, 45.6% had darkening of the skin, 25.3% had seborrhoeic inflamation of the skin, and 14.9% had eczema. Most of those whose skin had darkened were taking large doses of levomepromazine, and cornification was also correlated to large doses of psychotropic drugs. The seborrhoea, however, seemed to be associated with low dosages. Various theories about the reasons for this were debated. 35 references.

002922 Pantano, J. A.; Lee, Y.-C. no address **Acute coronary syndromes after sudden propranolol withdrawal: no evidence of a rebound hyperinotropic effect in healthy subjects.** Archives of Internal Medicine. 136:867, 1976.

Existence of a rebound hyperinotropic effect following sudden propranolol withdrawal was studied in healthy subjects. The 10 male and 11 female subjects ranged in age from 18 to 31 years. They were given propranolol, 30mg q.i.d. for 8 days. After exercise stress testing, those with a reduction in exercise heartrate greater than 20% were continued on the same dose for another 7 days, while the others took a dose of 40mg q.i.d. for the 7 day period. During the withdrawal period which followed, the systolic time intervals and 24 hour vanillylmandelic acid excretion did not differ from baseline levels.

002923 Piccaluga, G.; Vescovini, L. Instituti Ospedalieri Neuropsichiatrici S. Lazzaro, Reggio Emilia, Italy **/Discontinuance of associated antiparkinsonian drugs in long-term neuroleptic treatment./** La sospensione del trattamento associato con antiparkinsoniani nelle terapie protratte con neurolettici. Rivista Sperimentale di Freniatria (Reggio Emilia). 100(4):991-1005, 1976.

The validity of previous research concerning discontinuance of antiparkinsonian drugs given in association with long-term neuroleptic treatment was confirmed in 59 clinical cases. The patients, all females showing mainly chronic schizophrenia or some other chronic disease, were administered the antiparkinsonian agents triethylphenidil or orphenadrine for 2 months prior to the beginning of the double-blind test. All but 14 patients did not receive the antiparkinsonian drug for 1 month thereafter. Results showed that only three of the patients not receiving the antiparkinsonian had any side-effects following drug withdrawal, and that in no cases were there any changes in motor performance. 11 references.

002924 Poyen, B.; Jouglard, J.; Robaglia, J.-L. no address **/Suicide attempt in a subject treated with Idracilamide./** Observation d'une tentative de suicide chez un sujet traite par l'Idracilamide. Annales Medico-Psychologiques (Paris). 2(3):513, 1976.

A suicide attempt in a patient being treated with Idracilamide for a recurrent lumbago was reported at the 1976 session of the Societe de Psychiatrie de Marseille et du Sud-Est Mediterraneen. During the course of treatment with Idracilamide, the patient had had a succession of diverse psychiatric problems, culminating in the depressive episode which led to an overdose of barbiturates. The first episode had been a hypomania; the second, characterized by metamorphoses; and the third, a frank depression with ideas of ruination and guilt.

002925 Rampling, D. J. Department of Psychiatry, University of Adelaide, Adelaide, South Australia 5000, Australia **Imipramine and aggression.** Medical Journal of Australia (Glebe). 1(23):894-895, 1976.

A case of the onset of aggressive behavior in a paradoxical response to the tricyclic antidepressant, imipramine, by a man with a presumed disorder of the alerting mechanism is reported. The 26-year-old patient had suffered symptoms of narcolepsy and cataplexy since his teenage years and had suffered childhood poliomyelitis with encephalitic features. It is suggested that the cataplexy predisposed him to the drug reaction, and physicians are urged to be alert to central neurological dysfunction that could render a patient at high risk for such a response. 5 references.

002926 Reid, William H.; Blouin, Paule; Schermer, Michael. 1121 Paseo de Paralta, Santa Fe, NM 87501 **A review of psychotropic medications and the glaucomas.** International Pharmacopsychiatry (Basel). 11(3):163-174, 1976.

Four general groups of psychotropic drugs were examined with respect to possible adverse effects on intraocular pressure to support the hypothesis that systemically administered psychotropic medications, when given in recognized therapeutic doses and combinations, have no effect on the precipitation or exacerbation of glaucoma sufficient to warrant contraindication. The medication groups under consideration include phenothiazines, thioxanthenes, butyrophenones, monoamine oxidase inhibitors, tricyclic antidepressants, stimulants, antiparkinsonians, and antianxiety agents. After a brief discussion of the various mechanisms of glaucoma, information is provided concerning antipsychotic, antidepressant, antiparkinsonian, and antianxiety preparations of a variety of chemical structures and utilities. It is concluded that with certain basic safeguards, all of the medications studied are acceptably safe to prescribe even in patients with diagnosed glaucoma. It is recommended that although the prescription by the psychiatrist of any of the drugs discussed would result in a few serious ophthalmic complications, caution should be exer-

cised, especially in patients over 40 years old. A procedure that may be used to assess the chance of injury to a patient is offered. 58 references. (Author abstract modified)

002927 Rifkin, Arthur; Quitkin, Frederic; Klein, Donald F. Long Island Jewish-Hillside Medical Center, Glen Oaks, NY **Withdrawal reaction to diazepam.** Journal of the American Medical Association. 236(19):2172-2173, 1976.

A case of severe withdrawal reaction to a therapeutic dosage of diazepam is reported. A healthy 23-year-old man presenting moderate anticipatory anxiety symptoms underwent two grand mal convulsions within a 3 hour period, 5 days after being taken off the drug; his dosage had been only 10mg three times/day. A check with the manufacturer revealed that such severe withdrawal seizures are rare. Nevertheless, it is suggested that if benzodiazapines are given continuously for months, they should be withdrawn gradually. 2 references.

002928 Ruh-Bernhardt, D.; Finance, F.; Rohmer, F.; Singer, L. C.H.U. de Strasbourg, F-67005 Strasbourg-Cedex, France **/Effect of psychotropic therapy on thrombogenesis and on platelet functions: 4 cases of thromboembolic accidents occurring in patients treated with neuroleptics and antidepressants./** Incidence de la therapeutique psychotrope sur la thrombogenese et sur les fonctions plaquettaires. A propos de 4 cas d'accidents thromboemboliques survenus chez des malades traitees par neuroleptiques et antidepresseurs./ Encephale (Paris). 2(3):239-255, 1976.

Thromboembolic complications occurring as a result of psychotropic medication are discussed. Four female patients developed pulmonary emboli after being placed on the following psychotropic medications: 50mg/day clomipramine + 4.5mg/day lorazepam; 50mg/day clomipramine i.v. + 150mg/day clomipramine p.o.;metapramine; and 600mg/day lithium + 75mg/day Maprotiline chlorhydrate. The patients ranged in age from 57 to 76 years old. The 4 patients were found to have hyperaggregability of their platelets. 19 references.

002929 Saario, I. no address **/Diazepam impairs driving skills less than thioridazine./** And Diazepam rates better than thioridazine. British Journal of Clinical Pharmacology (London) 3:843, 1976.

Effects of diazepam and thioridazine on psychomotor skills related to driving were compared in 45 outpatients with anxiety. Compared with placebo, diazepam increased the number of mistakes in reaction and impaired coordination skills and flicker fusion discrimination, as did thioridazine. When the two drugs were compared, thioridazine was found to impair coordination, attention, and reactive skills more than did diazepam. Thioridazine in the doses used impairs driving skills more than diazepam, and thioridazine was also subjectively less effective treatment.

002930 Sakamoto, Fujio; Nagamatsu, Saburo; Kajiwara, Kagemasa; Sakamoto, Muneharu; Higashi, Katsumi; Kuroe, Ken; Hayashida, Masanori. Kirishima-Byoin National Sanatorium, Kagoshima Prefecture, Japan **A case presenting some reactive clinical signs during treatment of L-DOPA.** Iryo (Tokyo). 30(1):77-80, 1976.

The case of a 66-year-old male who showed L-DOPA reactive signs after being treated for Parkinsonism was reported. The patient died of pneumonia 20 days after admission, but prior to his death he demonstrated many reactive signs: gastrointestinal disturbances (nausea, vomiting, anorexia), neurological signs (involuntary movement, dizziness, tinnitus, sweating), cardiovascular disturbances (palpitation, dysrhythmia, flushing), and psychiatric signs (depressive episodes, hallucinations, vivid dreams, confusion, insomnia, somnolence). These signs developed a few days before admission. He had been receiving L-DOPA treatment for 12 months in an 800mg/day dosage. It was considered that these signs were not caused by the side-effects of L-DOPA directly, but developed indirectly subsequent to clinical signs, and that many factors were involved in their production. 19 references. (Journal abstract modified)

002931 Sato, Chikatsugi; Sugano, Keiju; Atsumi, Yoshinori; Atta, Kazunobu; Miyazaka, Matsue. Gunma Mental Hospital, Gunma, Japan **Transient dementia symptoms caused in one case by ethopropazine.** Psychiatria et Neurologia Japonica (Tokyo). 78(8):570, 1976.

In a paper presented at the 30th Northern Japan Psychoneurological Symposium held in September 1975 in Akita, Japan, the case of a 23-year-old depressed male who was afflicted with transient dementia caused by the side-effects of the major tranquilizer, ethopropazine, is reported. Dosage of ethopropazine was 450mg, or lesser dosages of that combined with hexyphenidyl plus promethazine, or trihexyphenidyl. Administration of the other drugs without ethopropazine, however, did not cause dementia. Upon withdrawal from ethopropazine his symptoms of mental impairment receded.

002932 Schou, Mogens. Psychopharmacology Research Unit, Psychiatric Hospital, DK-8240 Risskov, Denmark **What happened later to the lithium babies? A follow-up study of children born without malformations.** Acta Psychiatrica Scandinavica (Kobenhavn). 54(3):193-197, 1976.

The Lithium Baby Register was founded in 1968 to determine the frequency of abnormalities among children born to mothers who were given lithium during the first trimester of pregnancy. Previous studies have revealed an increased frequency of congenital malformations, possibly due to teratogenic action of lithium. The present report is a questionnaire followup of the physical and mental development of lithium children who were not malformed at birth. Sixty lithium children were examined; their siblings, who had not been exposed to lithium during fetal life, served as a control group. The data obtained do not reveal any increased frequency of physical or mental anomalies among the lithium children. 6 references. (Author abstract)

002933 Seppala, T. no address **/Lorazepam impairs driving skills./** Lorazepam impairs skills more than medazepam or diazepam. British Journal of Clinical Pharmacology (London) 3:831, 1976.

Effects of lorazepam, diazepam, and medazepam on psychomotor skills and visual functions related to driving were studied in 10 healthy volunteers. A single dose of 2.5mg lorazepam impaired almost all of the measured skills more than did 10mg diazepam or 15mg medazepam or placebo, while the magnitude and duration of impaired performance after diazepam fell between that of lorazepam and the slight effects of medazepam. There was no impairment of coordination skills after medazepam and only a slight increase in the inaccuracy of reaction mistakes. Patients should not drive for 24 hours after 2.5mg oral dose of lorazepam, while after a single dose of 10mg diazepam or 15mg medazepam, the impairment lasts 5 to 7 hours. The slow disappearance of lorazepam from the serum (it has a serum half-life of 12 hours) corresponds to its long duration of action.

002934 Simon, Norman M.; Garber, Elayne; Arieff, Alex J. Departments of Medicine and Neurology, Northwestern University Medical School, Chicago, IL 60611 **Persistent nephrogenic diabetes insipidus after lithium carbonate.** Annals of Internal Medicine. 86(4):446-447, 1977.

In a letter to the journal, a case history of a male manic-depressive who developed nephrogenic diabetes insipidus, as a side-effect of therapy with lithium salts was described. A 54-year-old man with a history of manic-depressive psychosis since age 19 had been treated with electroshock, insulin shock, tranquilizers, and antidepressant drugs. Lithium carbonate, 1200 to 1500mg daily, was prescribed for several years. This case was noteworthy because diabetes insipidus had previously been described as transient and reversible within weeks of cessation of treatment, but in this patient persisted for 20 months after the last chronic exposure to lithium carbonate. The mechanism of lithium induced diabetes insipidus has not been fully defined. However, both inhibition of vasopressin stimulated adenyl cyclase and of action of cyclic adenosine monophosphate have been shown in experimental studies. Pathologic and ultra structural renal changes have been noted in lithium treated rats with blood levels maintained in the therapeutic range recommended for man. 5 references.

002935 Simpson, George M.; Kline, Nathan S. Rockland Research Institute, Orangeburg, NY 10962 **Tardive dyskinesia: manifestations, incidence, etiology, and treatment.** In: Yahr, M., The basal ganglia. Vol. 55. New York, Raven Press, 1976. 474 p. (p. 427-446).

In a paper presented at the 55th meeting of the Association for Research in Nervous and Mental Disease, manifestations, incidence, etiology, and treatment of tardive dyskinesia, an extrapyramidal disorder associated with long-term neuroleptic therapy, were discussed. Contrary to its name, onset of the disorder need not be a late phenomenon and symptoms include Parkinsonian side effects. Prevalence figures vary from 0% to 40% of persons taking neuroleptics; other factors involved in etiology are age and sex, absolute amount of neuroleptic ingested, and presence of organicity. A substantial number of manics, misdiagnosed as schizophrenic, have developed dyskinesias on neuroleptic maintenance. Treatment modalities other than neuroleptics are usually preferable in nonschizophrenics, and widespread practice of polypharmacy probably has been influential in development of the disorder. The mechanism of production remains speculative, but has been hypothesized to be related to a dopamine hypersensitivity. Early diagnosis and treatment are critical, and lithium or deanol are the major drugs that have proven effective. Patients who have been on long-term neuroleptic treatment and develop a severe case of the disorder should have a slow withdrawal of medication. Preventive aspects are also indicated: neuroleptics should not be routinely used for affective disorders or neurotic states, and the smallest possible dosage should be employed in treating schizophrenia. In deeply psychotic cases, however, neuroleptics may still be the treatment of choice, and the dosage may be increased to overcome the tardive dyskinetic side-effect. 20 references.

002936 Spiker, Duane G.; Pugh, Daniel D. Department of Psychiatry, University of Pittsburgh School of Medicine 3811 O'Hare St., Pittsburgh, PA 15261 **Combining tricyclic and monoamine oxidase inhibitor antidepressants.** Archives of General Psychiatry. 33(7):828-830, 1976.

The charts of 150 inpatients and 51 outpatients treated with a monoamine oxidase inhibitor (MAOI) tricyclic antidepressant combination were reviewed to show the incidence and severity of side-effects among the patients on the combined regimen. The effects were essentially the same as those seen in the control groups. There were no deaths or strokes resulting from use of this regimen. The most frequent troublesome side-effect was orthostatic hypotension. It is indicated that the use of a MAOI tricyclic combination in oral therapeutic doses is safe. However, it is stated that the efficacy of this combination has not yet been proved, and it may be particularly toxic if taken in an overdose. 14 references. (Author abstract modified)

002937 Tachibana, Mitsuo; Tanaka, Katsuyuki; Hishikawa, Yasuo; Kaneko, Ziro. Department of Neuropsychiatry, Osaka University School of Medicine, Osaka, Japan **A sleep study of acute psychotic states due to alcohol and meprobamate addiction.** In: Weitzman, E., Advances in sleep research. New York, Spectrum, 1976. 236 p. (p. 177-205).

To study sleep occurring in acute psychotic states due to alcohol and drug addiction, polygraphic examination of the EEG, EOG, EMG, heartrate, and respiration was performed during nocturnal sleep in 11 alcoholics and three addicts who developed delirium, and in control Ss without overt psychotic symptoms. No significant difference was noted between the groups in percentage of stages 1, 3, 4, and stages REM. A large percentage of stage 1 and a markedly reduced value of stage 4 were common. An unusual sleep state characterized by concomitant appearance of low voltage, mixed frequency EEG activity, REM burst and tonic mental EMG was observed in alcoholics with delirium following alcohol withdrawal and delirium termination, termed 1-REM. Only a small amount of 1-REM occurred in alcoholics without overt psychotic symptoms, and alcoholics with hallucinosis occupied an intermediate position between those with delirium and those without psychotic symptoms. Stage 1-REM represented a large portion of total sleep time of addicts with delirium and was nearly absent in addicts with delirium. Stage 1-REM is considered a state caused by dissociated appearance of the phasic features of REM sleep from its tonic features. The pathologenic implications of the dissociation in development of delirium due to alcohol and meprobamate addiction are discussed. 41 references.

002938 Takeuchi, Tooru; Okuta, Gohei. Department of Neuropsychiatry, Takaoka Citizen's Hospital, Takaoka, Japan **A case where administration of lithium carbonate caused polyuria.** Psychiatria et Neurologia Japonica (Tokyo). 78(12):829-830, 1976.

At the 71st Psychoneurological Symposium of Northern Japan, held in June 1975, at Kanazawa, Japan, the case of a 27-year-old mentally retarded male who had experienced frequent mania for the past 10 years, and who exhibited polyuria from administration of lithium carbonate is reported. Administration of lithium carbonate in dosages of 1200mg/day caused urine volume to rise to from 5 to 10 liters daily. Urine volume returned to normal after cessation of the lithium. It was later readministered in conjunction with 50mg/day of hydrochlorothiazide and urine volume dropped, although it remained above normal.

002939 Tamminga, Carol; Smith, Robert C.; Chang, Sidney; Haraszti, Joseph S.; Davis, John M. Department of Psychiatry, University of Chicago, Chicago, IL 60637 **Depression associated with oral choline.** Lancet (London). No. 7991:905, 1976.

In a letter to the editor of Lancet, it is postulated that, since physostigmine reverses mania and pushes normal mood into severe transient depression, in depression there is a relative or

actual cholinergic hyperactivity. Increasing cholinergic load would thus increase the likelihood of depression, and depression would therefore be an expected side-effect of oral choline treatment. Two patients who became clinically depressed while taking choline for tardive dyskinesia are reported. It is concluded that since choline will continue to be used in the evaluation of movement disorders, awareness of depression as a possible side-effect of choline is warranted. 5 references.

002940 Trites, R. L.; Suh, M.; Offord, D.; Nieman, G.; Preston, D. Department of Psychology, University of Ottawa, Ottawa, Ontario, Canada **Neuropsychologic and psychosocial antecedents and chronic effects of prolonged use of solvents and methamphetamine. Part 1: group profiles.** Psychiatric Journal of the University of Ottawa (Ottawa). 1(1-2):14-20, 1976.

An investigation of chronic, cognitive, adaptive, motor, and sensory dysfunction associated with long-term use of volatile solvents is described, and preliminary results are presented. Subjects included 50 amphetamine users and 29 glue sniffers as well as matched siblings and schoolmate controls. All subjects had a 2 day neuropsychologic, neurologic, and psychiatric examination, and birth records and school records were assessed. Experimental subjects had been off drugs for 1 month, and were screened at each test through urine studies. Preliminary data indicate that Canadian and matched American drug user samples differ significantly in personality status. Consistent deficits on neurological examination were found in the amphetamine groups. 25 references. (Author abstract modified)

002941 Tverdova, Ye. B. Krymskaya oblastnaya psikhiatricheskaya bol'nitsa No. 1, Simferopol, USSR **/Glycemic side-effects in patients due to neuroleptic therapy./** Pobochnyy glikemicheskiy effekt u bol'nykh v rezul'tate lecheniya neyroleptikami. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova (Moskva). 76(3):450-452, 1976.

A study of causes of complications in combined insulin and neuroleptic therapy of schizophrenic patients showed that the neuroleptic drugs have properties that cause a drop in blood sugar, and have a latent side-effect on sugar metabolism. In long-term use of these preparations the sugar curves correspond to a latent and clinically expressed diabetes. It is concluded that cases of diabetes among mental patients are generally the result of long-term use of neuroleptic drugs. 1 reference. (Author abstract modified)

002942 Van Putten, Theodore; Crumpton, Evelyn; Yale, Coralee. Veterans Administration Hospital, Los Angeles, CA 90073 **Drug refusal in schizophrenia and the wish to be crazy.** Archives of General Psychiatry. 33(12):1443-1446, 1976.

The extremes of drug compliance were studied in two groups of schizophrenics: 29 habitual drug refusers who invariably discontinued medication only to be readmitted several months later, and 30 drug complier patients who habitually came in for their refills or injections of antipsychotic medication. The drug refusers experienced the resurgence of an ego syntonic grandiose psychosis after they discontinued medication. The habitual compliers, in contrast, developed decompensations characterized by such dysphoric affects as depression, anxiety, virtual absence of grandiosity, and some awareness of illness. The refusal of these chronic schizophrenics to take their medication could not be attributed to social isolation, paranoid diagnosis, or secondary gain. A discriminant function analysis showed grandiosity to be the most powerful discriminating variable between the two groups. These findings, to mean that some schizophrenics may prefer an ego syntonic grandiose psychosis to a relative drug induced normality. 12 references. (journal abstract)

002943 Wass, J. A. H.; Thorner, M. O.; Besser, G. M.; Morris, D.; Mason, A. Stuart; Liuzzi, A.; Chiodini, P. G. St. Bartholomew's Hospital, London EC1A 7BE, England **Gastrointestinal bleeding in patients on bromocriptine.** Lancet (London). No. 7990:851, 1976.

Gastrointestinal bleeding as a complication of therapy with bromocriptine is reported. Of 96 patients being treated with 10 to 60 mg/day bromocriptine for acromegaly, four developed peptic ulcer of the stomach and two developed peptic ulcer of the duodenum; three of these patients had severe gastrointestinal hemorrhages and two died, one from the bleeding and one following gastrectomy. Gastrointestinal bleeding was not encountered in any of 90 patients receiving bromocriptine for hyperprolactinemia, and it has not been reported in the use of bromocriptine for parkinsonism. It is suggested that patients be advised to take their bromocriptine with meals and to report relevant symptoms immediately.

002944 Wazek, Ya. Psikhiatricheskaya poliklinika OUNZ, Karlovy Vary, Czechoslovakia **/Extrapyramidal motor disturbances due to drug therapy of psychosis./** Ekstrapiramidal'nye dvigatel'nye rasstroystva, voznikayushchiye pri lechenii psikhozov lekarstvennymi sredstvami. Zhurnal Nevropatologii i Psikhiatrii imeni S. S. Korsakova (Moskva). 76(3):453-457, 1976.

Extrapyramidal motor disturbances as side-effects of the use of drugs (neuroleptics in particular) in the treatment of psychosis are reviewed in the literature. Various side-effects are listed, but it is concluded that modern psychopharmaceuticals are relatively safe if used correctly, serious complications being quite rare. 59 references.

002945 Weiser, G.; Dafalias, Ch.; Tahedl, A. Wagner-Jauregg-Krankenhaus, Wagner-Jauregg-Weg 15, A-4025 Linz, Austria **/Pseudopsychotic relapses in the course of long-term treatment with neuroleptics./** Vermeintliche Psychoserezidive im Verlaufe neuroleptischer Langzeitbehandlungen. Wiener Medizinische Wochenschrift (Wien). 126(32-35):484-489, 1976.

The phenomenon of the pseudorelapse in the schizophrenic patient receiving long-term antipsychotic medication is discussed. Such a relapse occurs, it is stated, not because of exacerbation of the schizophrenia itself, but because of neuropathological and psychopathological symptoms brought about by the psychotropic drugs. In one year, 65 such relapses were admitted to the Wagner-Jauregg Hospital in Linz, constituting 10.5% of all admissions of schizophrenics. The diagnoses of these patients covered the full range of the schizophrenias. Slightly more than half of these patients could be discharged within 12 weeks of admission. The symptoms of these patients included depression, hypokinesia or akinesia, akathisia, dyskinesia, and parkinsonism. The patients had been receiving a wide variety of antipsychotic medications. 17 references.

002946 Wencelis, Stanislaw. 33 Gliwicka ul., Rybnik, Poland **/Hemineurine abuse by a chronic alcoholic./** Naduzywanie hemineuryny przez chorego z alkoholizmem nalogowym. Psychiatria Polska (Warszawa). 10(6):695-698, 1976.

Abuse of hemineurine in chronic alcoholism is discussed, based on a case study of a 39-year-old male, married 15 years, with two children, who had been an alcoholic for 10 years. The significance of the social situation in tranquilizer abuse by

alcoholics is emphasized, and the toxic effects of the combination of drug and alcohol are stressed. 15 references.

002947 Wesson, Donald R.; Smith, David E. no address **Psychoactive drug crisis intervention.** Current Psychiatric Therapies. 16:203-208, 1976.

Techniques of psychoactive drug crisis intervention are described; symptoms of the following are discussed: 1) opiate or opioid overdose; 2) sedative/hypnotic overdose; 3) mixed opiate/sedative/hypnotic overdose; 4) acute stimulant reactions; 5) marijuana, hashish, and THC; and, 6) adverse psychedelic drug reactions. Four commonly used techniques of crisis intervention are identified: reassurance, taking over the crisis situation, education with additional information and/or resources, and relabeling the crisis (for example, family disruption may be the immediate crisis, rather than the perceived crisis of a family member's drug use). 2 references.

002948 Whyman, Andrew. Department of Psychological and Social Medicine, Pacific Medical Center, P.O. Box 7999, San Francisco, CA 94120 **Phenothiazine death: an unusual case report.** Journal of Nervous and Mental Disease. 163(3):214-217, 1976.

A case report of sudden, unexpected autopsy negative death in a hyperactive, hospitalized patient being treated with a modified schedule of rapid tranquilization is presented. The data of the study suggest that death was caused by phenothiazines and that phenothiazines can cause clinically significant depression of the medullary respiratory centers of the brainstem. It is concluded that clinicians should monitor rate and quality of respirations as well as blood pressure closely when schedules of rapid tranquilization are implemented. 17 references. (Author abstract modified)

002949 Wood, Charles A.; Brown, James R.; Coleman, James H.; Evans, William E. no address **Management of tricyclic antidepressant toxicities.** Diseases of the Nervous System. 37(8):459-461, 1976.

The pharmacological and toxicological rationale behind currently recommended treatment modalities of tricyclic antidepressants (TCA) is discussed. It is pointed out that metabolism of the TCA compounds occurs primarily in the liver. Amitriptyline, imipramine, and doxepin are demethylated to nortriptyline, desipramine, and desmethyl-doxepin, respectively. These demethylated metabolites are then inactivated in the liver and excreted as glucuronides in the feces and urine. The toxicities of TCAs are discussed as an extension of their pharmacological actions. The treatment of TCA toxicities is a multifaceted problem. The basic procedure involves: 1) administering physostigmine to treat life-threatening symptoms; 2) removing the drug from the stomach by emesis for gastric lavage; 3) administering activated charcoal for at least 24 hours; 4) taking general supportive measures; and 5) monitoring the patient's cardiovascular and respiratory systems. Careful attention to the potential problems coupled with adequate and speedy management should greatly improve the prognosis of the TCA overdose patient. 27 references.

002950 Yoshida, Noboru; Terashima, Masayoshi. no address **On changing blood densities of antiseizure drugs taken in large volumes.** Psychiatria et Neurologia Japonica (Tokyo). 78(6):471, 1976.

At the 89th Tokai Psychoneurological Symposium held in July 1975, at the Nagoya Public Hall, Japan, the blood serum levels of various antiseizure drugs in three patients who took large doses of them were measured and reported. Hospitalized cases showed high levels of both diphenylhydantoin and phenylbarbitol in the blood within the first few days of hospitalization after withdrawal; levels then began gradually falling off. In cases where a high dosage of the drugs was used, serum levels fell off to the same level as in those patients who had taken lower dosages. The consciousness impairments noted by these patients, however, took longer to subside for those who had taken the higher dosages. It was concluded that the consciousness impairments noted by users of these drugs could not be correlated with the serum levels of the drugs in their blood.

002951 Zdichynec, B. OUNZ Pelhrimov, Interni Oddeleni NsP, Pocatky, Czechoslovakia **/Side-effects of some psychochemotherapeutic drugs on systemic circulation in atherosclerosis and in somatically healthy, elderly persons./** Vedlejsi ucinky nekterych psychofarmak na krevni obeh u aterosklerozy a u somaticky zdravych osob pokrocilejsiho veku. Ceskoslovenska Psychiatrie (Praha). 72(4):265-273, 1976.

Side-effects of some psychopharmaceuticals in atherosclerotics and in physically healthy, elderly persons are described. Undesirable circulatory reactions may develop after administration of doses routinely given in so-called minor psychiatry. Characteristic clinical symptoms can be objectivized by investigating some of the EKG parameters and the autonomic equilibrium (sympathetic irritability is increased, the Schellong test shows hypodynamic or even hypotonic reaction). Drugs which may be administered to elderly persons or to patients with atherosclerosis are oxazepam, diazepam, prothiaden, thioridazine and amitriptyline in low doses. Relatively unsuitable are: levopromazine, chlorpromazine, nortriptyline. Mellipramine (imipramine) should not be used at all. If the relatively unsuitable psychopharmaceuticals have to be administered, EKG and the orthoclinostatic test should be monitored. The hypotensive side-effect of amitriptyline can be applied in combination with rauwolfia in the treatment of some hypertensive conditions. 19 references.

16 METHODS DEVELOPMENT

002952 Abrams, Richard. University Psychiatric Service, Department of Psychiatry and Behavioral Science, SUNY at Stony Brook, Stony Brook, NY **Psychopharmacology and convulsive therapy.** In: Wolman, B., The therapist's handbook: treatment methods. New York, Van Nostrand Reinhold, 1976. 539 p. (p. 18-45).

Guidelines for the use of the various psychopharmacologic and convulsive therapies in the treatment of mental illness are presented. It is emphasized that successful drug therapy results from administration of active compounds in sufficient doses of suitable preparation, by an effective route of administration, and for an adequate time period. The neuroleptic drugs, whose two main classes include the tricyclics and butyrophenones, are used in treating excitement and overactivity in acute mania or schizophrenia. Anxiolytic drugs, which share the relaxant, anticonvulsant, central depressant, and addicting properties of the barbiturates, are widely used for anxiety reduction and nighttime sedation in neurotic patients. Lithium has no central sedative or tranquilizing properties but is specifically active in patients with manic-depression. The two main classes of antidepressants (tricyclics and monoaminoxidase inhibitors) have different structures, chemical properties, and clinical indications. Convulsive therapy, used extensively in treating depression and also with schizophrenia, and organic psychoses may be combined with drugs to shorten the treat-

ment course. Techniques for administering induced seizures are similar and include bilateral and unilateral electroconvulsive therapy (ECT) inhalant induction with flurothyl and regressive ECT. 97 references.

002953 Anweiler, J.; Bender, G.; Hobel, M. Pharmakologisches Institut der Universitat, Im Neuenheimer Feld 366, D-6900 Heidelberg 1, Germany **Simultaneous determination of glutethimide, methyprylon, and methaqualone in serum by gas liquid chromatography.** Archives of Toxicology (Berlin). 35(3):187-193, 1976.

A gas chromatographic method is described that permits the simultaneous determination of glutethimide, methyprylon, and methaqualone in serum samples. The method is sufficiently sensitive, the threshold for the three compounds being 0.2mg/l. No interaction with metabolities of any of the three substances was observed. Since the analysis of one serum sample takes approximately 1 h, the method is suitable for diagnostic use in stuporous patients suspected of having ingested one or more of these three hypnotics. 14 references. (Author abstract modified)

002954 Bein, H. J. Research Department, Pharmaceuticals Division, Ciba-Geigy, Basel, Switzerland **Some facets of the screening of psychopharmacological agents.** In: Advances in the drug therapy of mental illness. Geneva, World Health Organization, 1976. 168 p. (p. 33-36).

The principles of evaluation of new drugs and recent methodological trends are discussed in reference to problems on spectra of drug action. It is pointed out that although chlorpromazine, reserpine, and imipramine were initially developed on the strength of clinical observations, they were also notable for their potent effects produced in animal experiments. The result has been a tendency towards the pragmatic approach with efforts being concentrated upon the search for analogues showing formal similarity of effect in individual test systems. The actions of clomipramine, impramine, desipramine, and maprotiline are compared. Lithium and polypeptides are also discussed. 7 references.

002955 de Groot, G.; Maes, R. A. A.; Lemmens, H. H. J. Center for Human Toxicology, University of Utrecht, Vondellaan 14, Utrecht, The Netherlands **Determination of lorazepam in plasma by electron capture GLC.** Archives of Toxicology (Berlin). 35(3):229-234, 1976.

A method is described for the determination of lorazepam plasma levels involving extraction from the sample and analysis of the intact lorazepam by electron capture gas liquid chromatography. Using mass spectrometry it is demonstrated that lorazepam shows a thermal rearrangement under gas chromatographic conditions. The limit of detection is 0.01mg/l and the assay shows a linearity from 0.01-0.80mg lorazepam per liter of plasma. Under the described conditions the method is well adapted both for the determination of very low plasma levels as appearing in the transplacental transfer of lorazepam and in samples from patients who have taken an overdose of lorezepam. 15 references. (Author abstract modified)

002956 Kennedy, Patricia Margaret. Fordham University, New York, NY **Pharmacological testing in a correctional institution: the impact of content variables on willingness to volunteer, personality adjustment and informed consent. (Ph.D. dissertation).** Dissertation Abstracts International. Ann Arbor, MI, Univ. M-films, No. 76-17931 HCS15.00 MFS8.50 166 p.

The influence of certain content variables in pharmacological research on the self-perceptions, motivations, and informed consent recall of penitentiary inmate volunteers was researched. Content variables were status of the target disease being investigated and the nature of the informing procedures was employed. Self-perception variables were favorable and unfavorable descriptions, personal adjustment, aggression, anxiety, depression, and degree of purposefulness. It was hypothesized that: 1) inmates in the high (heart), middle (ulcer), and low (cold) status conditions would be differentiated hierarchically with respect to increases in positive self-esteem, personal adjustment, and degree of purposefulness, and decreases in aggression, anxiety, and depression; 2) inmates in the three status conditions would be differentiated in motivations for volunteering; and 3) inmates in the standard, group audiovisual and programmed text formats for informed consent would be differentiated with respect to degree of recall of informed consent material, and significant interaction effect would be obtained between informed consent format and disease status condition. The results from testing Ss with the Adjective Check List, State-Trait Anxiety Inventory, Beck Depression Inventory, Purpose-in-Life Test, and a semantic differential for health questionnaire did not support the hypotheses. Volunteers as a whole had decreased anxiety in comparison with nonvolunteer controls. The tentative nature of the results were emphasized, since they were obtained from a pilot study. (Journal abstract modified)

17 MISCELLANEOUS

002957 Aberg, Hans. Department of Medicine, University Hospital, Uppsala, Sweden **The use of propranolol in somatic medicine.** In: Carlsson, C., Neuro-psychiatric effects of adrenergic beta-receptor. Munich, Urban & Schwarzenburg, 1976. 120 p. (p. 29-34).

In a paper presented at a symposium on neuropsychiatric effects of adrenergic beta-receptor blocking agents held in Copenhagen, October 1975, contraindications, dosages, and side-effects of the use of beta-blocking agents in somatic medicine are discussed. The experience of physicians over the past ten years indicates that risk is not great. Adverse reactions in 129 of 1500 patients in one reported study is thought to be representative; these, however, were distributed over a wide range of diagnostic categories. It is concluded that, while much remains to be learned, the introduction of beta-blocking drugs represents one of the more important advances in somatic medicine in recent times, particularly in the field of cardiovascular disorders. 20 references.

002958 Adomakoh, C. C. Department of Psychiatry, University of Ghana Medical School, Accra, Ghana **Studies on the clinical evaluation of psychotropic drugs.** In: Advances in the drug therapy of mental illness. Geneva, World Health Organization, 1976. 168 p. (p. 11-14).

Problems and difficulties that might detract from the usefulness of clinical trials of psychotropic drugs or impede their execution are identified. It is pointed out that all evaluation methodology has inherent difficulties. The areas discussed include: criteria for delineating the disorder, choice of subjects, range of dosage, drug interactions, measurement of criteria of improvement, social factors, and duration of trials. It is concluded that clinicians must improve their skills in order to evaluate the many drugs developed for the treatment of mental disorders. 4 references.

002959 Airaksinen, M. University of Kuopio, Kuopio, Finland **Proceedings of the Sixth International Congress of Pharmacology Volume 3: CNS and behavioural pharmacology.** Elmsford, New York, Pergamon Press, 1976. 344 p. v.3. $50.00.

The papers presented at the Sixth International Congress of Pharmacology held in Helsinki, Finland in July, 1975 are presented in book form. Special reports concerning the use of drugs in wild animals and the involvement of pituitary peptides in motivational, learning, and memory processes are presented. Papers dealing with various aspects of alcohol dependence include discussions of: 1) the adaptive changes in membranes which may be associated with the development of dependence: 2) the effects of ongoing behavior on the magnitude of physical dependence; 3) genetic factors in the response to alcohol in mice; 4) the effects of ethanol on biogenic amines; 5) the use of alcohol as a reinforcer in operant behavior studies; and 6) studies of the dose relationships for alcohol dependence in humans. Other papers report studies of the interactions of neurotransmitters and hypothalamic releasing hormones, some of which pertain to the neuronal control of gonadotropin secretion. A third group of papers deals with the criteria and methods used to study the effects of drugs on the emotions in animals and the applicability of the results for the use of drugs to treat emotional disturbances in humans. The final group of reports deals with studies of the levels of monoamine metabolites in the cerebrospinal fluid as related to the etiologies of affective illness and schizophrenia and the selective effects of psychoactive drugs in these illnesses.

002960 Altman, J. L.; Albert, J.-M.; Milstein, S. L.; Greenberg, I. INRS-Sante, Universite du Quebec, Hopital L.H. Lafontaine, Montreal, Quebec, Canada **Drugs as discriminative events in humans.** Psychopharmacology Communications. 2(4):327-330, 1976.

At a symposium on the research aspects of drug induced discriminative stimuli conducted in connection with the annual meeting of the Behavioral Pharmacology Society, Durham, New Hampshire, in May 1976, a tabulation of studies dealing with drugs as discriminative events in humans was presented. One table lists experiments in which subjects attempted to identify either the class of substance or the specific drug received. A second table lists studies examining the ability of subjects to recall material associated with a drug (or nondrug) state when retested under the same or different drug conditions. 29 references. (Author abstract modified)

002961 Andolfi, Maurizio; Menghi, Paolo. Societa Italiana di Terapia Familiare, Rome, Italy **/Prescription in family therapy: part 1./** La prescrizione in terapia familiare. I. Archivio di Psicologia, Neurologia E Psichiatria (Milano). 37(4):434-456, 1976.

The use of psychopharmacotherapeutic prescription in family therapy is defined and analyzed to demonstrate how effective it can be in bringing about changes in family attitude and behavior toward a mentally ill member of the family. Several family cases are described, in which therapy lasted for 3 to 6 months, with the therapist meeting with the family on a weekly basis. It is concluded that the use of psychopharmacotherapy prescription as a technique or strategy can be most useful, whether of the restructuring or paradoxical type, and can bring about rapid behavior modification in the mentally disturbed subject if the families cooperate effectively. 21 references.

002962 Angst, J.; Woggon, Brigitte. University Psychiatric Clinic, Zurich, Switzerland **Pharmacological treatment of affective disorders.** In: Advances in the drug therapy of mental illness. Geneva, World Health Organization, 1976. 168 p. (p. 15-22).

An overview of the pharmacological treatment of affective disorders is presented. Treatment of depressive episodes, recent developments in tricyclic and tetracyclic antidepressants, and prediction of the outcome of treatment are discussed. It is concluded that, despite the recent failure to develop more effective antidepressant drugs, the prospect for future progress is encouraging. This prospect is characterized by the following points: 1) the breadth of the spectrum of active treatment; 2) a loosening of pharmacological criteria in the screening of antidepressant drugs; 3) a higher chemical variability of the compounds tested; 4) promising attempts to find predictors of clinical response; 5) the development of further multidimensional methods for the assessment of drug induced changes in the clinical picture. 42 references.

002963 Bangham, A. D. Institute of Animal Physiology, Babraham, Cambridge, England **Alcohol, anaesthetics, mem-**

branes. In: Airaksinen, M., CNS and behavioural pharmacology. Elmsford, New York, Pergamon Press, 1976. 344 p. v. 3. (p. 33-39).

In a paper presented at the Sixth International Congress of Pharmacology held in Helsinki, Finland in July, 1975, factors which might affect the action on biological membranes of alcohol, general anesthetics, or other drugs having the potential to produce physical dependence are discussed. Membrane permeability is dependent upon the concentration of foreign molecules present, to temperature, and to the pressure on the system. A hypothesis for anesthetic action based upon changes of the Gibbs free energy which might result in a membrane consequent to the addition of foreign molecules, a change of temperature, a change of pressure, or a combination of these variables is proposed. A change in ground state free energy which would diminish the change in Gibbs free energy would enhance permeability, possibly interfering with normal tissue functioning. It is suggested that ethanol acts as one of a class of anesthetic agents that act on membranes and that dependence may arise by an adaptive change in the membrane itself. The disorder caused by the primary drug action may be offset in the dependent state by a change in the lipid components of the membrane, producing a membrane that functions normally only in the presence of the drug. 12 references.

002964 Barry, Herbert, III; Krimmer, Edward C. Dept. of Pharmacology, University of Pittsburgh School of Pharmacy, Pittsburgh, PA 15261 **Discriminable stimuli produced by alcohol and other CNS depressants.** Psychopharmacology Communications. 2(4):323-326, 1976.

At a symposium on the research aspects of drug induced discriminative stimuli conducted in connection with the annual meeting of the Behavioral Pharmacology Society, Durham, New Hampshire, in May 1976, discriminable stimuli produced by alcohol and other CNS depressants were briefly reviewed with emphasis on their use in evaluation of sedative and antianxiety agents in rats. Though some drug induced changes may occur slowly, they are pervasive, stable, and distinctive. Alcohol may be an appropriate prototype for the discriminative stimulus effects of the sedative and antianxiety agents because of the consistent choice of the discriminative alcohol response in tests with pentobarbital and chlordiazepoxide. The high degree of generalization of the alcohol stimulus to these other drugs may be attributable to the more pervasively depressant actions of alcohol or its weaker discriminative stimulus attributes. 6 references.

002965 Berger, F. M. Department of Psychiatry, University of Louisville School of Medicine, Louisville, KY **Aminergic factors in mental illness.** In: Essman, W., Current developments in psychopharmacology. New York, Spectrum, 1976. 393 p. v. 3. (p. 125-153).

Theories of the physical bases for schizophrenia, affective disorders, and psychoneurotic illness resulting from studies of the biochemical and behavioral effects produced by drugs which are capable of inducing or alleviating mental disturbances are discussed. Biochemical events involved in the biosynthesis and catabolism of norepinephrine (NE), dopamine (DA), and serotonin (5-hydroxytryptamine, 5-HT) are reviewed, and the effects of various drugs which interfere with them, including antipsychotics (phenothiazines and butyrophenones), amphetamine, hallucinogens, tricyclic antidepressants, monoamine oxidase inhibitors, and lithium, are briefly summarized. Among the topics discussed are: 1) the exacerbation or induction of psychotic symptoms in schizophrenia by methionine, tryptophan, L-DOPA, amphetamine, methamphetamine, and methylphenidate; 2) the induction of hypomanic behavior in bipolar manic-depressive illness by L-DOPA; 3) the ability of amphetamine to induce paranoid psychoses in normal subjects; 4) the ability of lysergic acid diethylamide to induce abnormal mental states in normal subjects; 5) the ability of reserpine or parachlorophenylalanine to induce depression in normal subjects; 6) the methylation hypothesis, which proposes that schizophrenia is the result of a faulty biochemical mechanism producing a disturbance in the methylation of biogenic amines; 7) the hypothesis that schizophrenia is due to a disturbance of cerebral DA metabolism; 8) the theory that schizophrenia is due to disturbances of the metabolism of tryptophan or 5-HT; 9) the catecholamine hypothesis of affective disorders, which postulates that depression and mania result from a deficiency of NE and an excess of NE, respectively, at cerebral receptors; 10) the 5-HT hypothesis of depression, which postulates a causal relationship between depression and cerebral 5-HT deficiency; and 11) hypotheses of the involvement of acetylcholine in depression. The hypothesis that psychoneurotic diseases are related to increased reactivity of interneurons and that anxiolytics act by reducing this reactivity is also discussed and it is pointed out that no biochemical changes having a causal relationship with psychoneurotic disease have been defined. 96 references.

002966 Berger, G.; Kohl, U. Stadtische Krankenanstalten, Nurnberg Psychiatrische und Nervenklinik, Flurstrasse 17, 8500 Nurnberg, West Germany **/Identical psychosis in a pair of monozygotic twins./** Identische Psychose bei einem eneiigen Zwillingspaar. Fortschritte der Neurologie, Psychiatrie etc. (Stuttgart). 44(6):373-378, 1976.

The case of two 29-year-old German females, monozygotic twins with a close lifelong relationship who were admitted to a hospital with endogenous psychosis characterized by hallucinations and delusions of persecution, is reported in detail. Although upon admittance only one of the twins received neuroleptic medication, both twins recovered simultaneously and at the same rate; trained psychiatrists were unable to distinguish the twin receiving medication from the untreated twin. The case histories, the history of similar and dissimilar treatment, the special effects of the twins' symbiotic relationship, the nature of the shared delusions and hallucinations, and the results of intelligence and personality tests administered are described. 19 references.

002967 Bianchine, Joseph R. Department of Pharmacology, Ohio State University College of Medicine, 333 W. Tenth Avenue, Columbus, OH 43210 **Drug therapy of Parkinsonism.** New England Journal of Medicine. 295(15):814-818, 1976.

Drug therapy of Parkinsonism is examined briefly, focusing on selected factors which are thought to contribute to the therapeutic outcome when levodopa is administered. The mechanism of action when levodopa, dopa decarboxylase inhibitors, or amantadine is used is explained, as are toxicity and side-effects, effects of long-term treatment, and clinical use of levodopa. Two phases of treatment with levodopa, the induction phase and the mentenance phase, are distinguished. Anticholinergic drugs, now largely relegated to a supportive role in Parkinsonism treatment, are discussed briefly. 12 references.

002968 Binder, S.; Doddabela, P. Landeskrankenhaus Eickelborn, D-4780 Lippstadt-Eickelborn, Germany. **Efficacy of piracetam on mental functional capacity of chronic alcoholics.** Med. Klin. 71:711-716, 1976.

In a double-blind crossover study, piracetam, 1-pyrrolidone acetamide, was tested by means of psychological tests in 40 chronic alcoholics with some degree of marked psychoorganic syndrome. Statistical analysis of the results showed that piracetam improved the energofunctional capacity of the cortex or basal functions of the cortical cells (activating capacity, vital dynamic, flexibility, intellectual reactivity, and stress tolerance). Apart from overall improvement, enhanced specific cerebral performances were noted. (Journal abstract modified)

002969 Bisio, Bruno. Ospedale Psichiatrico Provinciale di Ascoli Piceno in Fermo, Ascoli Piceno, Italy **/Clinical therapeutic reports on addiction to rare drugs./** Riferimenti clinico-terapeutici in tema di tossicomanie rare. L'Ospedale Psichiatrico (Napoli). 44(2):195-217, 1976.

Drug addiction to meprobamate and olantin in ten clinical cases is examined following a brief overview of the use of drugs in Italy, to dramatize the contention that true drug addicts have genuine personality disorders and that taking drugs gives them relief from pain or displeasure. Two cases of meprobamate addiction in females and eight clinical patients who became addicted to dolantin are clinically evaluated. It is concluded that meprobamate drug addiction usually occurs after having taken the drug for therapeutic purposes with slow but eventual complete dependence upon the drug. With dolantin, originally used as a substitute for morphine and as a pain killer, the subject not only becomes acutely addicted to the drug but cannot eat or sleep without his drug dosage. Final recommendation is that both drugs be administered only by physicians to prevent addiction. Additionally, although sleep therapy, electroschock, and insulin therapy have been tried, especially with dolantin addicts, results have been inconclusive. 39 references.

002970 Blackburn, J. L.; Laxdal, O. E.; Dempsey, M. J. College of Pharmacy, University of Saskatchewan, Saskatoon, Sask. S7N 0W8, Canada **Saskatchewan dial-access drug information service.** Canadian Medical Association Journal (Ottawa). 115(9):869-871, 1976.

The implementation, operations, and preliminary evaluation of a dial access drug information service for physicians and pharmacists in Saskatchewan are described. The system was added in September 1974 to an already existing dial access tape library service which began in 1970 at the University of Saskatchewan. Operating without charge and with the use of a radio page system, calls are taken immediately by experienced pharmacists and pharmacologists. The cost of long distance phone charges is borne by grants from the Saskatechwan medical and pharmaceutical associations. The operating cost of the service during its first 12 months was less than $3000. During the first year of operation, 415 requests for information were received. Of the 93 persons who called up to February 28, 1975, 76% responded to an evaluation questionnaire; virtually all respondents described the service as very valuable. The information received resulted in the alteration of drug therapy in one third of the calls requesting information to assist in the current patient treatment. Future modifications of the system and cost/benefit analyses are described. 12 references. (Author abstract modified)

002971 Blum, Kenneth. Department of Pharmacology, University of Texas Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 78284 **Depressive states induced by drugs of abuse: clinical evidence, theoretical mechanisms and proposed treatment. Part II.** Journal of Psychedelic Drugs. 8(3):235-262, 1976.

A review of the literature is presented with regard to three types of commonly abused drugs: narcotics (heroin and methadone), CNS stimulants (amphetamines and cocaine) and CNS depressants (barbiturates, minor tranquilizers and alcohol). Emphasis is placed on the mechanisms by which these drugs induce depression during use or abstinence. Possible modes of treatment including the use of tricyclic antidepressants and monoamine oxidase inhibitors, are suggested. For each group of drugs, the following subjects are reviewed: 1) clinical evidence of depression; 2) mechanisms for induction of depression (catecholamine theory, serotonin theory); and 3) theories of manifestation of clinical depression. 163 references.

002972 Bojdecki, Krzysztor. II Klinika Psychiatryczna, Instytut Psychoneurologiczmej, Warsaw, Poland **/Application of beta-receptor blocking agents in combined therapy of endogenous psychosis./** Zastosowanie zwiazkow blokujacych beta-receptory w skojarzonej terapii psychoz endogennych. Psychofarmakoterapia Schizofrenii Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 197-204).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, application of beta-blockers in combined therapy of endogenous psychosis is reviewed. Review of the literature and clinical observations confirm the beneficial use of beta-blockers as a corrective drug in pharmacological treatment of psychoses. 26 references.

002973 Boulenger, J.-P.; Brion, S. Centre Hospitalier, 1, rue Richaud, F-78000 Versailles, France **/Interaction of alcohol with psychotropic drugs./** Interactions alcool-medicaments psychotropes. Encephale (Paris). 2(4):325-340, 1976.

Alcohol/psychotropic drug interactions are outlined. Following a brief review of the metabolic and pharmacological properties of ethanol, the principal types of alcohol/drug interaction are listed, including: pharmacological interactions affecting the central nervous system, metabolic interactions including mainly stages of oxidation in the liver, and clinical interaction involving acute and chronic alcoholic intoxication. Problems presented by interaction of ethanol with various psychotropic drugs are outlined, including: anxiolytics, antidepressants, neuroleptics, and barbiturates. It is cautioned that the personality of the patient is perhaps more important than the consumption of drugs. 78 references.

002974 Bovet, D. Laboratorio di Psicologia e Psicofarmacologia, Rome, Italie **/Spectrum of activity of some drugs./** Spectre d'action des medicaments. In: Advances in the drug therapy of mental illness. Geneva, World Health Organization, 1976. 169 p. (p.37-42).

The spectra of activity of several drugs is presented. The following topics are discussed: 1) the important recent developments in neurochemistry, neuroendocrinology, and neurophysiology, and the possibilities for pharmaceutical research; 2) the possibilities offered by research on animal behavior; and 3) chemical therapy of mental illness. It is pointed out that decisive progress has been made by the introduction of psychotropic medicines in the treatment of manic-depressives. Unresolved problems in the treatment and prevention of numerous other psychiatric afflictions are also considered. 43 references.

002975 Bridges-Webb, Charles. Department of Community Medicine, University of Sydney, New South Wales 2006, Australia **/Alleged psychotropic drug use in the elderly./** Comment 3. Medical Journal of Australia (Glebe). 2(2):67-68, 1976.

A defense of appropriate drug prescription for the elderly is offered in response to "Psychotropic Drug Use in the Elderly: Public Ignorance or Indifferent?" by Simon F. Chapman. It is pointed out that increased drug use among the elderly is partly due to the fact that most diseases, including mental disorders, are more severe and chronic in the elderly. In addition, increasing use of psychotropic drugs may reflect the fact that more patients are using medical services. Chapman's point that the social situations underlying the health problems of the elderly must be tackled is supported, but it is argued that in the meantime, the medical practitioner must offer symptomatic relief and support, and psychotropic drugs are one means of doing so. The great volume of prescribing does not mean that drugs are the only means being used. 5 references. (Author abstract modified)

002976 Brodersen, P. E.; Mikkelsen, B. O. Faaborg Sygeh, Faaborg, Denmark. **Treatment of disturbances of sleep with flurazepam, nitrazepam, and allypropymal.** Ugeskr. Laeger. 138:88-90, 1976.

In a double-blind clinical trail comprising 130 patients, a newer benzodiazepine (flurazepam) was compared with a known benzodiazepine (nitrazepam) and a known barbiturate (allypropymal). To assess the hypnotic effect the following parameters were compared: time required to fall asleep, duration of sleep, ability to sleep throughout the night, condition on waking, and the quality of sleep. The investigation did not reveal any statistically significant difference among the three preparations as regards the parameters investigated. There was a tendency, however, for those taking allypropymal to need a longer time to fall asleep.

002977 Carlsson, Arvid. Department of Pharmacology, University of Goteborg, Fack, S-400 33 Goteborg, Sweden **Central catecholamines.** In: Carlsson, C., Neuro-psychiatric effects of adrenergic beta-receptor. Munich, Urban & Schwarzenburg, 1976. 120 p. (p. 1-5).

In a paper presented at a symposium on neuropsychiatric effects of adrenergic beta-receptor blocking agents held in Copenhagen, October 1975, it is contended that beta-adrenergic mechanisms are present in the brain. Two lines of evidence are cited: 1) a demonstration of a dopamine sensitive adenylate cyclase system in the caudate nucleus; this system can be activated by dopamine, and this effect is blocked by neuroleptic drugs such as phenothiazines and butyrophenones; and 2) the discovery of an isoprenaline sensitive adenylate cyclase in the caudate nucleus which can be blocked by beta-adrenergic blocking agents, indicating the presence of beta-adrenergic receptor mechanisms in the caudate nucleus. The difficulty of proving the presence of such mechanisms is thought to be that the other receptor mechanisms in the brain are so dominating. Cathecholamine synthesis is discussed in general terms.

002978 Carlsson, Carl; Engel, Jorgen; Hansson, Lennart. Department of Pharmacology, University of Goteborg, Fack, S-400 33 Goteberg, Sweden **Neuro-psychiatric effects of adrenergic beta-receptor blocking agents.** Advances in Clinical Pharmacology, v. 12. Munich, Urban & Schwarzenberg, 1976. 120 p.

Proceedings from a symposium on the neuropsychiatric effects of adrenergic beta-receptor blocking agents held in Copenhagen, Denmark, October 1975, critically reviewed these agents and offered an interchange of ideas and opinions on their therapeutic application among leading neuropsychiatric experts. Topics covered included: central catecholamines; the psychopharmacology of beta-adrenergic blockade; psychosomatics of anxiety; prophanolol in alcoholism, stammering, tremors, and anxiety; metabolics of schizophrenia; and beta-adrenergic blocking agents in the treatment of psychoses.

002979 Cervantes Leon, Gregorio. no address **/Psychopharmacological research./** Investigacion Farmacopsiquiatrica. Neurologia - Neurocirugia - Psiquiatria (Mexico City). 17(3):129-131, 1976.

A statement of the proper method of performing psychotropic drug trials in human subjects is offered. The first phase in clinical testing consists of trials on normal humans to test tolerance once the toxicology and animal pharmacology tests have determined the drug's biological activity. The second phase consists of early testing on normal volunteers and later on patients in order to verify the biological predictions for the drug. The third phase is carried out on significant clinical samples. The need for adequate and formal control of the testing is emphasized in the light of the many published trials which include serious errors in methodology, and which sometimes utilize false statistics and spurious correlations. Researchers are advised that, while the work of colleagues must be respected, published drug trials must be read critically.

002980 Chapman, Simon F. Central Drug and Alcoholic Advisory Service, P.O. Box 160, Rozelle, New South Wales 2039, Australia **Psychotropic drug use in the elderly: public ignorance or indifference?** Medical Journal of Australia (Glebe). 2(2):62-64, 1976.

Statistics on psychotropic drug use among the elderly are presented, and socially based reasons for such use are suggested. Australian data show that drug consumption by the elderly is greatly overproportionate to their representation in the population. It is suggested that the volume of psychotropic drugs is not due to the propensity of the elderly to decline with age but to the total situation of the elderly person in society. Societal attitudes, poverty, and isolation can increase the physical and emotional manifestations of decline, which are, in turn, reflected in the volume of drug use. 11 references. (Author abstract modified)

002981 Coppen, Alec; Perris, Carlo. Medical Research Council, Neuropsychiatry Laboratory, West Park Hospital, Epsom, Surrey, England **Trials with antidepressants reassessed.** International Pharmacopsychiatry (Basel). 11(3):175-180, 1976.

Factors important for the valid evaluation of new antidepressant drugs are reviewed, emphasizing the fact that the course of affective disorders must be understood before any proper prospective view on the value of a particular treatment can be obtained. It is suggested that antidepressant drugs should be tested in clearly defined groups of patients, with consideration given to patients who drop out of trials and the number of patients in a treatment program. Additionally, the drugs should be tested in optimum doses for the patient, preferably with plasma levels of the drug regularly monitored. Comparison should be double-blind, against placebo or a standard drug given in optimum dosage. Finally, rating scales should be reliable and sensitive. It is concluded that lack of attention to these principles could lead to the marketing of drugs of doubtful and unproven benefits to patients. 10 references.

002982 Covi, Lino; Lipman, Ronald S.; Smith, Virginia K. NIMH, Parklawn Building, 5600 Fishers Lane, Rockville, MD 20857 **The effect of sequence on the stability of the Hopkins Symptom Checklist (HSCL). (Unpublished paper).** Rockville, MD, NIMH, 1976. 12 p.

In a study undertaken to determine the effect, if any, of change in sequence in administering the Hopkins Symptom Checklist (HSCL), a patient self-rating scale for evaluating psychopharmacotherapeutic agents, 142 outpatients of a psychiatric clinic were administered the HSCL, half before and half after an initial evaluation interview. Study results indicate that when the HSCL is administered using the timeframe "the past 7 days, including today", the influence of the initial interview on the level of distress is insignificant. No interaction of diagnosis with sequence was found, while differences in reported distress in the three largest diagnostic groups were present. These findings contrast sharply with three previous studies where the timeframe was specified as "right now."

002983 Czerniak, P.; Zwas, S. T. Department of Nuclear Medicine, Sheba Medical Center, Tel Hashomer, Israel **/Use of radioactive copper and radioactive zinc in psychiatric diagnosis./** Usage du radiocuivre et du radiozinc pour le diagnostic psychiatrique. Annales Medico-Psychologiques (Paris). 1(4):566-577, 1976.

The metabolism of copper and zinc in normal controls and psychiatric patients, studied by means of Cu-64 and Zn-65, is discussed in a paper presented at the November 24, 1975 meeting of the Societe Medico-Psychologique. For the copper metabolism study, Cu-64 was given i.v. and orally to 25 healthy volunteers, 15 patients with Wilson's disease, and 50 patients with psychiatric problems, and copper concentration was determined in the blood, in urine and feces, and in the liver and brain over the next 3 days. The pattern of copper distribution in the patients with Wilson's disease permitted a diagnosis of this entity. The 17 male and 33 female psychiatric patients ranged in age from under 20 to over 60. Diagnoses were schizophrenia in 35, anxiety reaction in 9, and hysteria in 6. Cerebral uptake of copper was elevated in the patients with schizophrenia and anxiety compared with the hysteria patients and the normals. Albino mice, albino rats, and schizophrenia patients all showed an increased uptake of zinc by the brain following treatment with chlorpromazine, thioridazine, and perphenazine. 14 references.

002984 de Barbenza, Claribel M. Departamento de Psicologia, Universidad Nacional de San Luis, San Luis, Argentina **/Functions of loud sound, personality, and drugs./** Funciones de sonoridad, personalidad y drogas. Revista Latinoamericana de Psicologia (Bogota). 8(2):283-293, 1976.

To determine whether individual perception of loudness may vary with the personality of the perceptor and with the administration of a central stimulant (amphetamine sulfate) or depressor (medazepam) 40 subjects were evaluated for personality factors and tested with active agents and a placebo. The Eysenck Personality Inventory, Taylor's Anxiety Scale, and the Harris AC Creativity test were used to evaluate the individual personalities. Highly creative and highly introverted subjects had greater sensibility to loudness and more exquisite discrimination of sounds than other groups at significant levels. The two drugs did not appear to alter sound perception in any subject, regardless of personality characteristics. 14 references.

002985 De Rios, Marlene Dobkin; Smith, David E. Department of Anthropology, California State University, Fullerton, CA 92631 **Using or abusing? An anthropological approach to the study of psychoactive drugs.** Journal of Psychedelic Drugs. 8(3):263-266, 1976.

An historical approach is taken to develop the following definition of drug abuse: the use of a psychoactive substance in a fashion that seriously interferes with the economic, physical or social functioning of the user. As such it is contended that the ritual use of drugs is not drug abuse. It is contended that the major danger in the use of drugs for ritualistic purposes is that the user may be arrested for drug abuse. A call for more research in this area is made. 18 references.

002986 Donlon, Patrick T.; Stenson, Randall L. Department of Psychiatry, School of Medicine, University of California, Davis, CA 95616 **Neuroleptic induced extrapyramidal symptoms.** Diseases of the Nervous System. 37(11):629-635, 1976.

The four general forms of extrapyramidal symptoms (EPS) frequently associated with neuroleptic therapy (pseudoparkinsonism, akathisia, acute dystonic reactions and tardive dykinesia) are discussed in terms of their signs and symptoms, their appearance and course, their differential diagnosis, incidence, determinants and treatment. These EPS are a function of biological sensitivity, neuroleptic molecular structure, dose, age, sex, and duration of neuroleptic treatment. Because of their association with EPS, at times irreversible, and their modest efficacy in the nonschizophrenic patients, neuroleptic administration should be limited predominantly to schizophrenic patients. Furthermore EPS should not be used as a guideline for the efficacy of neuroleptics as formerly assumed. For EPS may occur at subtherapeutic doses of neuroleptics and may be absent in patients experiencing clinical response. Neuroleptic dose should be the lowest efficacious dose required to provide symptom remission. In addition, antiparkinsonian (AP) agents should be administered predominently contractively and not routinely in combination with neuroleptics. With the judicious administration of neuroleptic agents and AP medication, distressing EPS can be prevented or minimized, while providing control of schizophrenic symptoms. 21 references. (Author abstract modified)

002987 Ellinwood, Everett H., Jr.; Petrie, William M. Behavioral Neuropharmacology Section, Department of Psychiatry, Duke University Medical Center, Durham, NC **Amphetamine and cocaine abuse. (Unpublished paper).** Rockville, MD, NIMH, 1976. 38 p.

The abuse of amphetamine-like stimulant drugs and cocaine is discussed. Among the topics included are: 1) a historical account of cocaine use and abuse; 2) pharmacological effects and behavioral effects produced by stimulant abuse; 3) the development of tolerance to stimulants; 4) the occasional use of stimulants by students and athletes; 5) intravenous use of stimulants; 6) concomitant use of other drugs, including barbiturates and narcotics, with stimulants; 7) the development of psychosis associated with chronic stimulant usage; 8) the potential for chronic high dose use of stimulants to produce violent behavior; 9) the ability of stimulants to activate preexisting psychopathology; 10) the effects of stimulants in laboratory animals, including rodents and primates; and 11) emergency treatment of toxicity and overdosage, stimulant psychosis, and withdrawal symptoms. 88 references.

002988 Engelhardt, David M.; Polizos, Polizoes. Downstate Medical Center, 450 Clarkson Avenue, Brooklyn, NY 11203 **Adverse effects of pharmacotherapy in childhood psychosis.** Research Report, NIMH Grant MH-26960, 1976. 20 p.

Adverse effects of pharmacotherapy in childhood psychosis were studied in 95 outpatient of pharmacotherapy in childhood psychosis were studied in 95 outpatient subjects with diag-

noses of childhood schizophrenia with autistic features. It was found that adverse effects presented no serious problems during treatment; in most instances side-effects diminished or disappeared in the course of treatment or could be controlled by dose reduction or contramedication. The profile of treatment emergent side-effects was similar to that observed in adults, except that children showed greater incidence of increased salivation and dystonia and had greater potential for developing neurological symptoms on discontinuation of drug treatment. Despite clinical stabilization, most children experienced clinical relapse within 1 to 2 weeks after discontinuation of neuroleptic therapy, thus differing from adult schizophrenics, who often maintain their improved status. Children maintained on pharmacotherapy for prolonged periods were judged not to have suffered any serious deleterious developmental effects from chronic drug administration. 30 references. (Author abstract modified)

002989 Essman, Walter B.; Valzelli, L. Department of Psychology, Queens College of the City University of New York, Flushing, NY **Current developments in psychopharmacology.** New York, Spectrum, 1976. 393 p. Vol. 3.

A variety of recent developments in the field of psychopharmacology are reviewed. These include: 1) studies of the induction of amnesia by drugs in mice and by electroconvulsive therapy in man, and the implications of these studies for the biology of memory; 2) findings concerning the nature of the behavioral deficits produced by cycloheximide and hypotheses explaining the mechanisms by which the deficits are produced; 3) studies of the effects of various dopaminergic drugs on serotonin (5-hydroxytryptamine) neurons which lead to the hypothesis of a dopaminergic/serotonergic interaction in the CNS; 4) the effects of neurotransmitters and the pharmacological agents that affect them on pituitary function; 5) theories of biochemical bases for psychiatric disorders and mechanisms by which drugs can induce or alleviate mental disturbances; 6) the involvement of sodium ion in the development and course of lithium intoxication in rats; 7) the use of psychotropic drugs, especially antidepressants, for suicide prevention in depressed patients; 8) studies on aggression induced by drugs and on the role of various neurotransmitters in the mediation of this effect; and 9) physiological mechanisms involved in integrative activity of the brain, with emphasis on the telencephalic contribution in higher mammals and on the effects of piracetam.

002990 Glick, S. D.; Goldfarb, J. no address **Behavioral pharmacology.** St. Louis, C. V. Mosby, 1976. $16.95.

Behavioral Pharmacology, an edited collection of chapters rather than singly authored text, is intended to introduce behavioral pharmacology to those readers with a minimal background in the parent disciplines. Chapters on experimental psychology; on the anatomy, physiology, and chemistry of the nervous system; and on basic pharmacology serve as an introduction to later chapters dealing with the effects of drugs on schedule controlled behavior, on arousal and consummatory behavior, on sexual and aggressive behavior, and on learning and memory. More specialized chapters deal with drug addiction, changes in drug effects due to nervous system damage, and with animal models used in drug screening. The book attests to the partnership between experimental psychology and pharmacology that gave rise to the field of behavioral pharmacology which has changed the approach to explanations of drug actions. It also highlights the fact that behavioral pharmacology is a distinct discipline from others that study the effects of drugs having primary effects on the central nervous system. It is not the same as neuropharmacology or neurochemistry, even though interested in many of the same drugs. Behavioral pharmacology focuses on the behavioral effects of drugs. 4 references.

002991 Gottfries, Carl Gerhard. Psykiatriska kliniken, Lasarettet, S-901 85 Umea, Sweden **/Annual meeting of the Scandinavian Association of Psychopharmacology./** Skandinavisk selskab for psykofarmakologi. Nordisk Psykiatrisk Tidsskrift (Kungsbacka). 30(7):487-490, 1976.

The program of the annual meeting of the Scandinavian Association of Psychopharmacology is presented. The 210 participating pharmacologists, psychiatrists, and representatives from the medical industries gathered for 2 days in Copenhagen, in March 1976 to discuss long-term treatment with neuroleptic drugs, and long-term treatment with tricyclic antidepressants. Principles for long-term treatment of schizophrenic patients as well as secondary effects of neuroleptic drugs were presented. Results from animal studies of tardive dyskinesia were also reported. Some speeches were concerned with the correlation between the plasma concentration of tricyclic antidepressants and their clinical effects.

002992 Graham, J. D. P. no address **Cannabis and health.** New York, Academic, 1976. 481 p. L14.50.

A review of the effects of cannabis use on mental and physical health is presented. The nature of cannabis and cannabinoids is examined in over 350 published pharmacological reports; and physiological and behavioral aspects of cannabis consumption are discussed. Chemistry and pharmacognosy and social and legal issues surrounding the use of the drug are examined. Cannabis is examined in terms of criteria used in the certification of other drugs for public use, and it is concluded that uncertainties about long-term effects would probably preclude its distribution without prescription.

002993 Guigou, G. Interne des Hopitaux, Sainte-Marguerite, Marseille, France **/Placebo methods./** Les methodes placebo. Psychologie Medicale (Paris). 8(8):1216-1222, 1976.

Discussion at the 4th Methodology of Research in Psychiatry Meeting held in Marseille, April 1975 explored the effectiveness of placebo methods. The principle of placebo is defined as an attempt to neutralize, in pharmacology, nonspecific variables. Clinical perspectives consider: 1) the role of placebo for the researcher and patient; 2) its quality; 3) the methods which utilize it; 4) the corpus; 5) the phenemona which are considered; and 5) ethical and socioeconomic aspects, and the role cultural reference. Placebo methods contribute to a better understanding of the personality of the therapist, to an increased rigor in clinical studies, and to clarifying the relations between psychiatry and fundamental disciplines whose accomplishments are not yet obvious.

002994 Harthoorn, A. M. Transvaal Nature Conservation Division, Pretoria, South Africa **Psychopharmacology and conservation.** In: Airaksinen, M., CNS and behavioural pharmacology. Elmsford, New York, Pergamon Press, 1976. 344 p. v.3. (p. 3-17).

In a paper presented at the Sixth International Congress of Pharmacology held in Helsinki, Finland in July 1975, the use of drugs in the capture and relocation of wild animals is discussed with emphasis on the chemical restraint of free living wild animals and the alleviation of fear, anxiety, and depression during captivity. Brief observations on wild animal behavior are presented and the variations in that behavior

which may affect drug dosage and experimental results as well as the effects of the drug on behavior itself are discussed. Specific topics presented include: 1) drug effects as related to the animal's state of excitation; 2) the relationship between conditioning (habituation to a stimulus) and drug effects; 3) suppression of avoidance behavior by drugs enabling an animal to be approached; 4) nutritional status, water intake, and metabolism as factors affecting drug dosage; 5) genetic factors affecting drug dosage; and 6) selection of drugs for various species. The predictability of drug effects from one species to another, from domestic animals, and from man to wild animals is also discussed. 15 references.

002995 Heinrich, K. no address **/Psychotropic drugs in the clinic and in practice./** Psychopharmaka in Klinik und Praxis. Stuttgart, Georg Thieme, 1976. 123 p. DM12.80.

A comprehensive reference manual of pharmacopsychiatry with indications for practical application is presented. Psychotropic drugs are discussed in appropriate groups, together with reported effects and side-effects.

002996 Hippius, Hans. University Psychiatric Clinic, Munich, Federal Republic of Germany **The concept of "target symptoms" for drug treatment in psychiatry.** In: Advances in the drug therapy of mental illness. Geneva, World Health Organization, 1976. 168 p. (p. 79-82).

The concept of target symptoms is defined and a brief history of the symptoms oriented approach and the disease oriented approach to drug treatment is presented. It is suggested that the concept of target symptoms should be modified to a concept of target structure, taking into consideration: 1) the cross-section of psychopathological symptomatology; 2) the course of the illness; 3) the nosological context of symptomatology; and 4) the inclusion of more biological, especially biochemical and neurophysiological, parameters. It is concluded that such a concept of target structures would be of increasing importance for differential indications for various methods of treatment, of increasing value for predicting the outcome of a treatment, and a useful instrument in psychiatric research. 11 references.

002997 Iversen, Leslie L.; Iversen, Susan D.; Snyder, Solomon H. University of Cambridge **Handbook of psychopharmacology.** New York, Plenum, 1976.

An encyclopedic overview of the neurological, biochemical, metabolic, physiological, and behavioral aspects of psychopharmacology and drug therapy is presented. Section 1, comprising volumes 1-6, reviews and evaluates the state of the art in basic neurochemistry and neuropharmacology. Section II reports on neurotransmitter specific pathways in the brain which mediate the effects of many psychotropic drugs and describes and evaluates the experimental analysis of drug induced behavioral alternatives. Section III, emphasizing clinical pharmacology, focuses on the major classes of psychopharmaceuticals. (Journal abstract modified)

002998 Johnson, Anita. no address **FDA: a slow starter and a slow runner.** Trial. 12(10):22-25, 1976.

Inadequacies of drug research and of the Food and Drug Administration (FDA) as an arbiter of the consumer safety of pharmaceuticals are discussed. The major problem is seen to be the unavoidable bias of preclinical and clinical screening of drugs by manufacturers. Research results by drug firms upon which FDA decisions are based are found to often be inaccurate, uncritical, or biased in methodology. An example of biased reporting of research results involving Abbott Laboratories' attempt to suppress unfavorable findings on the effectiveness of magnesium pemoline for the management of hyperkinesis is presented. FDA reaction to hazardous products is described as "extended paralysis," and it is suggested that the FDA often does not remove carcinogenic products from the market or require a warning on the label, despite laws giving them authority to act. It is felt that a strong proconsumer lobby is needed to insure that the FDA works in the interest of public health and safety based on the increasing public concern for drug safety and more accessible data for the public and their advocates.

002999 Johnson, D. A. W. University Hospital of South Manchester, West Didsbury, Manchester M20 8LR, England **The expectation of outcome from maintenance therapy in chronic schizophrenic patients.** British Journal of Psychiatry (London). 128:246-250, 1976.

The results from a prospective followup study of a group of schizophrenic patients suggest that a significant proportion (41%) are likely to relapse during a 2 year period despite the prescription of long-acting injectable neuroleptic drugs. Some will relapse because of a failure of the regime, but others (32 to 37%) because the pharmacological protection of these drugs would appear to be less effective in certain patients. Even with the major advantages of the long-acting injectable neuroleptics over oral medication, the schizophrenic patient population remains a group with a high incidence of psychiatric and social morbidity which continues to require the full resources of both the hospital and community services. 17 references. (Author abstract)

003000 Kanemori, Ken. no address **Pharmacotherapy and medical insurance.** Psychiatria et Neurologia Japonica (Tokyo). 78(8):576, 1976.

In a paper read at the 30th Northern Japan Psychoneurological Symposium held in September 1975 in Akita, Japan, the effect of patient medical insurance on psychopharmacology in mental hospitals is discussed. In Japan, where doctors' fees from medical insurance are determined to some extent by drug prescription, it is pointed out that income from outpatient medication is much higher than for inpatient pharmacotherapy. This is true for all categories of drugs. Abolition of this system of doctor fee determination for outpatient drug prescription is advocated.

003001 Kirikae, Tatsuo. Department of Psychiatry, Iwate University, Iwate Prefecture, Japan **The present state of pharmacotherapy.** Psychiatria et Neurologia Japonica (Tokyo). 78(8):575-576, 1976.

In a report to the 30th Northern Japan Psychoneurological Symposium held in September 1975 in Akita, Japan, a survey of 20 treatment facilities' use of psychotropic drugs in Iwate Prefecture, Japan is described. Some results of the survey indicated that 68 patients were given pharmacotherapy for schizophrenia, 40 for manic-depression, 20 for epilepsy, and 20 for neurosis. The percentage of use of the various drugs for each disease is also reported. Conclusion is reached that with the combined use of various drugs, and doubts pertaining to their effectiveness and their side-effects, a reevaluation of pharmacotherapy programs in Japan is in order.

003002 Krimmer, Edward C.; Barry, Herbert, III. Dept. of Pharmacology, University of Pittsburgh School of Pharmacy, Pittsburgh, PA 15261 **Discriminable stimuli produced by marihuana constituents.** Psychopharmacology Communications. 2(4):319-322, 1976.

At a symposium on the research aspects of drug induced discriminative stimuli conducted in connection with the annual meeting of the Behavioral Pharmacology Society, Durham, New Hampshire, in May 1976, the discriminable stimuli produced by marihuana constituents was briefly reviewed with emphasis on specific discrimination in experimental animal models. Delta9-tetrahydracannabinol (THC) produces discrimination in rats and gerbils regardless of administration route, though response time varies. A diverse assemblage of compounds including a wide variety of depressants, stimulants, hallucinogens, neurotransmitter antagonists, narcotics, narcotic antagonists, and cannabinoid antagonists do not elicit the specific THC response. It is concluded that cannabis products are a unique group of compounds that do not fit into any known category. 2 references.

003003 Kuhn, D. M.; White, F. J.; Appel, J. B. Behavioral Pharmacology Laboratory, Dept. of Psychology, University of South Carolina, Columbia, SC 29208 **Discriminable stimuli produced by hallucinogens.** Psychopharmacology Communications. 2(4):345-348, 1976.

At a symposium on the research aspects of drug induced discriminative stimuli conducted in connection with the annual meeting of the Behavioral Pharmacology Society, Durham, New Hampshire, in May 1976, discriminable stimuli produced by hallucinogens, including lysergic acid diethylamide (LSD), psilocybin, mescaline, ditran, and phencyclidine were reviewed with emphasis on transfer tests and antagonism studies. It is concluded that the ability of an hallucinogen to serve as a discriminative stimulus per se does not indicate hallucinogenic liability in man. Although the discrimination properties of LSD and possibly mescaline appear to be mediated by serotonin receptors, preliminary studies have suggested that it might be more accurate to attribute the mediation of the stimulus properties of LSD to an LSD (rather than a 5-HT) receptor. 15 references.

003004 Lal, Harbans. Dept. of Pharmacology and Toxicology, University of Rhode Island, Kingston, RI 02881 **General characteristics of discriminative stimuli produced by drugs.** Psychopharmacology Communications. 2(4):305-309, 1976.

Generalizations from data presented at a symposium on the research aspects of drug induced discriminative stimuli (DS) conducted in connection with the annual meeting of the Behavioral Pharmacology Society, Durham, New Hampshire, in May 1976, are presented. The data reveal that: 1) a large number of groups of drugs, including anesthetics, sedative hypnotics, anxiolytics, narcotic analgesics, muscarinic cholinergic agonists, nicotinic cholinergic agonists, cholinergic antagonists, dopamine receptor agonists, amphetamines, psychotomimetics, marihuana constituents, antidepressants, and neuroleptics, produce DS; 2) DS produced by most drugs are characteristic of their drug class; 3) DS are very specific actions of drugs which are produced at dose levels that do not markedly affect behavioral rates; 4) discrimination can be formed to a specific action of a drug where other actions of the same drug may be ignored; 5) drug induced stimuli are distinct sensations which are unlike the sensations produced by usual sensory stimuli; 6) certain drugs can produce two distinct stimuli based upon the dose used for discrimination training; 7) tolerance to the DS produced by drugs is not seen except under certain experimental conditions using narcotic analgesics; 8) the stimulus control of behavior as exerted by drug stimuli usually follows the same rules of learning as have been established with physical stimuli of external origin; and 9) DS are perceived in both laboratory animals and humans. The research applications of drug induced discriminative stimuli are briefly discussed. 1 reference.

003005 Lal, Harbans; Gianutsos, Gerald. Dept. of Pharmacology and Psychology, University of Rhode Island, Kingston, RI 02881 **Discriminable stimuli produced by narcotic analgesics.** Psychopharmacology Communications. 2(4):311-314, 1976.

At a symposium on the research aspects of drug induced discriminative stimuli (DS) conducted in connection with the annual meeting of the Behavioral Pharmacology Scoiety, Durham, New Hampshire, in May 1976, the DS produced by narcotic analgesics was reviewed. Animals trained to discriminate one narcotic from vehicle will discriminate all other narcotic drugs from other psychotropic drugs or nonnarcotic analgesics. The narcotic stimulus is readily antagonized only by specific narcotic antagonists such as naloxone. Tolerance may be developed to the narcotic stimulus but can be minimized by continuing discrimination training during the repeated injections. Narcotic induced DS can also be conditioned to environmental stimuli. It is concluded that narcotic drugs produce narcotic specific stimuli which can be readily perceived by laboratory animals and which form the basis for behavioral control. The rank order potency of narcotics in producing a discriminable stimulus shows a high correlation with analgesia. The site of action of these discriminable stimuli is within the central nervous system, and several properties of these stimuli resemble those attributed to narcotic specific euphoria which is known to be subjectively perceived by the habitual user of narcotic drugs. 7 references. (Author abstract modified)

003006 Leeds, Alice A. Psychopharmacology Research Branch, National Institute of Mental Health, Rockville, MD **Ethics in drug research in the USA.** In: Advances in the drug therapy of mental illness. Geneva, World Health Organization, 1976. 168 p. (p. 107-111).

Societal ethics in drug research, particularly in human experimentation are examined in terms of civil rights and federal regulations. It is suggested that interpretation of existing laws is influenced by political pressures. Although concern for the civil rights of individuals has always been foremost in the minds of responsible investigators working in clinical trials, preservation of human rights and the advancement of medicine have often collided. Proposed guidelines, and the creation of review boards and protection committees to protect individual rights are outlined.

003007 Lefroy, R. B. Salvatori House, 35 Outram Street, West Perth, Western Australia 6005, Australia **/Alleged psychotropic drug use in the elderly./** Comment 2. Medical Journal of Australia (Glebe). 2(2):66-67, 1976.

The tendency to overprescribe psychotropic drugs for the elderly is criticized in a comment on "Psychotropic Drug Use in the Elderly: Public Ignorance or Indifference?" by Simon F. Chapman. It is pointed out that psychological symptoms, notably depression, increase during later life, but it is an error to assume that all symptoms must or can be treated by drugs. Two conditions must exist before overprescribing will end: there must be a realization that elderly people react to drugs differently from younger people, and there must be an alternative to the treatment of psychological symptoms with drugs. Physical, mental, and social factors often combine to produce symptoms. It is noted that there is a resistance to the need for geriatric medicine, yet training in this area would lead to greater understanding of use of drugs and consequently fewer prescriptions. 2 references. (Author abstract modified)

003008 Lehmann, Heinz, E. Medical Education and Research, Douglas Hospital, Montreal, Quebec, Canada **Interactions of drugs and other approaches in the treatment of the mentally ill.** In: Advances in the drug therapy of mental illness. Geneva, World Health Organization, 1976. 168 p. (p. 112-121).

The interactions of pharmacotherapy with three other therapeutic approaches are discussed in order to identify specific research questions. Physical treatments considered in relation to drug treatment are: fever therapy hypoglycaemic coma, prefrontal lobotomy, and electroconvulsive therapy (ECT). The first two approaches are not discussed in detail. Five areas related to interactions of pharmacotherapy with ECT discussed are: 1) ECT considered as an addition to or substitute for drug treatment; 2) ECT with or without drugs; 3) the appropriate number of ECT sessions; 4) drugs which should be used after ECT; and 5) definite contraindications for the simultaneous administration of ECT and certain drugs. 30 references.

003009 Lewi, Paul J. Research Laboratories, Janssen Pharmaceutica NV, B-2340 Beerse, Belgium **Clinical and pharmacological spectral maps of the neuroleptics.** International Pharmacopsychiatry (Basel). 11(3):181-189, 1976.

The degree of predictivity and concordance between various mapping techniques for neuroleptic compounds is described. It is posited that the clinical and pharmacological activity spectra of the neuroleptics can be projected into a map where compounds with similar spectra, but with possibly different potencies, are grouped together. Further, the spectral maps were devised for classification and for the prediction of therapeutic effects from pharmacological observations. It is concluded that specific correlations can be observed within and between pharmacological and clinical classifications. Pharmacological maps appear to be one dimensional and resemble the Lambert incisive/sedative bipolar scale. The Liege clinical physiognomy of neuroleptics shows an additional component which may be related to antimanic/antiautistic effects. 21 references. (Author abstract modified)

003010 Lewi, Paul J.; Colpaert, Francis C. Research Laboratories, Janssen Pharmaceutica NV, B-2340 Beerse, Belgium **On the classification of antidepressant drugs.** Psychopharmacology (Berlin). 49(2):219-224, 1976.

Clinical, pharmacologic and biochemical profiles of the actions of antidepressant drugs in animals and in humans have been analyzed statistically. A method derived from multivariate statistics separates drug potency from the spectral information contained in the profiles. The dimensionality of the spectra is reduced, resulting in a diagram of associations and dissociations between the antidepressants and their scales of observation. The spectra of antidepressants show three poles which have been labeled as D (desipraminelike), A (amitriptylinelike), and M (monoamine oxidase inhibitors). Better agreement is found between clinical spectra than among pharmacologic spectra. MAOI are readily differentiated from the tricyclic compounds. The clinical spectra by which the tricyclic compounds are ranked along the D to A bipolar axis produce the sequence desipramine, nortriptyline, imipramine, and amitriptyline. The same order of ranking is also produced from biochemical spectra of central blockade and peripheral blockade of norepinephrine reuptake and serotonin uptake. 21 references. (Author abstract modified)

003011 Lopez-Ibor Alino, J. J. Departamento de Psiquiatria de la Universidad e Salamanca, Salamanca, Spain /**Therapeutic actions of the neuroleptics and their influence in the psychopathology of schizophrenia.**/ Acciones terapeuticas de los neurolepticos y su influencia en la psicopatologia de la esquizofrenia. Neurologia Psiquiatria y ciencias afines (Madrid). 4(2 Etapa, 3):171-180, 1976.

The relationship between the therapeutic actions of neuroleptics and the effects of these drugs on the pathologic processes of schizophrenia are explored. It is suggested that the extrapyramidal side-effects of neuroleptics may be integrally bound up with their favorable action. They create a psychological distance in the patient between aberration and normal behavior. In schizophrenia, it is admitted that the diagnosis is still difficult, particularly the differentiation of schizophrenia from essential depressions and from manic-depressive episodes. Once diagnosed, it must be remembered that depression, febrile catatonic occurrences, respiratory problems, and fever are often concomitants of schizophrenia itself, and should not be invariably regarded as side-effects of the neuroleptic drugs. Even Parkinson like syndromes may be an indication of neurotic depression or of certain senility reactions. Nonetheless, at least the factor in this study is called "syndrome mutation," or changes in the patient seen only when receiving neuroleptic medication, is quite probably a side-effect of the drug. 58 references.

003012 Manku, M. S.; Horrobin, D. F. Clinical Research Institute, Montreal, Quebec, Canada **Chloroquine, quinine, procaine, quinidine, tricyclic antidepressants, and methylxanthines as prostaglandin agonists and antagonists.** Lancet (London). No. 7995:1115-1117, 1976.

The possibility that prostaglandins are important in several situations in which their role has so far been unsuspected is disucssed. It is pointed out that chloroquine, quinine, procaine, quinidine, clomipramine, theophylline, and caffeine have been shown to be strong prostaglandin antagonists and weak agonists. The antagonist effect is clearly demonstrable at concentrations reached in human plasma when the drugs are used therapeutically. A working hypothesis is suggested that these drugs and others related to them are active because they are prostaglandin agonists and antagonists. Clinical uses of the drugs and their mechanisms of action are described. Clinical implications are discussed and it is felt that new approaches to the development of prostaglandin antagonists and new uses for established drugs are indicated. For example, a preliminary study shows that chloroquine has been successfully used to close patent ductus arteriosus in three infants. 84 references. (Author abstract modified)

003013 Masserman, Jules H. no address **Experimental and clinical vectors in pharmacology.** Current Psychiatric Therapies. 16:107-116, 1976.

Experimental evidence regarding the variable effects of psychoactive drugs on the genetic, physiologic, socioexperiential, and environmental polysystems of human beings is reviewed. Animal neurophysiologic studies indicated that the functions of cerebral centers and neural tracts differ significantly among species and are greatly affected by the individual's unique experiences. Drug effects in humans and animals are shown to vary correspondingly with constitutional, experiential, and ambient factors. Human neuropharmacology is discussed with reference to dopamine, the polypeptides, tricyclic drugs, norepenephrine, and the benzodiazepines. Suggestive effects of medication are discussed. It is concluded that attention should be given to the specific effects of a psychotropic drug on the individual patient. 57 references. (Author abstract modified)

003014 Mattila, M. no address **Modern problems of pharmacopsychiatry. Vol. II: alcohol, drugs and driving.** Basel, S. Karger, 1976. 102 p. $19.00.

The outcome of a symposium on Alcohol, Drugs, and Driving held in Helsinki in 1975 is presented. Subjects covered in this volume include: the efficacy of law enforcement procedures, validity of breathalyzers, driving habits of hospital patients, and examination of the effect of alcohol on variables involved in braking reactions. The effect of tranquilizers on driving skills and their interaction with alcohol, the role of alcohol in nontraffic pedestrian accidents, and the consistency of accident rates in professional driving population are also discussed.

003015 Miyakoshi, Takashi. no address **The ethics and the actualities of pharmacotherapy.** Psychiatria et Neurologia Japonica (Tokyo). 78(8):576, 1976.

In a paper presented at the 30th Northern Japan Psychoneurological Symposium held in September 1975 in Akita, Japan, the ethical questions involved in and the limitations to psychopharmacology are discussed. It is argued that severe limitations on prevention of relapse of mental illness, and real curing of mental illness are seen in pharmacotherapy. Criticism is leveled at the medical establishment for its overwillingness to try out new miracle drugs when no reasonable hope for effects can be expected. Strict controls of pharmacotherapy administration and a reevaluation of the ethics of this therapy are called for. More research is also advocated into the long-term effects of this therapy and into the side-effects experienced by past patients.

003016 Modestin, J. Psychiatrische Universitatspoliklinik, Murtenstrasse 21, CH-3010 Bern, Switzerland **/Beta-receptor blockers in psychiatry./** Beta-Rezeptorenblocker in der Psychiatrie. Fortschritte der Neurologie, Psych. und ihrer Grenzgebieta (Stuttgart). 44(10):579-596, 1976.

The clinical literature on the use of beta-adrenergic blocking agents in psychiatry is reviewed. Among the clinical conditions discussed are the use of these drugs in functional cardiovascular disorders, anxiety, emotional stress, drug dependence, psychoses, tremors, and other disorders. Beta-adrenergic blockers cause depression and psychotoxicity as side-effects. The principal indications of beta-adrenergic blocking agents in psychiatry seem to be functional cardiovascular disorders and "somatic" anxiety. Among the beta-adrenergic blockers examined were propranolol, alprenolol, pindolol, oxprenolol, niphenalol, and practolol. 179 references.

003017 Myslobodsky, Michael; Weiner, Murray. Neurobiology Unit, Department of Psychology, Tel-Aviv University, Ramat-Aviv, Tel-Aviv, Israel **Pharmacologic implications of hemispheric asymmetry.** Life Sciences (Oxford). 19(10):1467-1478, 1976.

Differences in individual sensitivity to drugs that may relate to hemispheric asymmetric patterns are discussed. Several mechanisms may contribute to the unequal influence of systemically administered drugs on each hemisphere, including effect of hemispheric activity status on speed and degree of local uptake of drug, differential in synaptic sensitivity, and degree of competition with local endogenous neurohumors. It is suggested that it may be preferable to administer some drugs only at night or only in the daytime and preferably during periods of controlled mental activity or against a background of accompanying external manipulations. Few studies of drug efficacy have considered these variables as deserving control. The data and concepts reviewed suggest that the asymmetric nature of cerebral function and metabolic events should no longer be ignored in evaluating the disposition and activity of centrally active drugs. 66 references. (Author abstract modified)

003018 Nagurska, Hanna; Tyszka, Ewa; Wojdyslawska, Irena. Klinika Psychiatryczna, Akademia Medyczna, Lodz, Poland **/Results of schizophrenia treatment over a five-year period./** Wyniki leczenia schizofrenii w swietle piecioletniej katamenzy. Psychofarmakoterapia Schizofrenii Leki o Przedluzonmy Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 117-120).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, results of pharmacotherapy of schizophrenia over a 5 year period are presented. Evaluations are based on controlled observations made by physicians and on subjective evaluations by the patients. The study took into account the type and time of treatment during the first hospitalization, outpatient treatment, environmental factors, and the quality of systematic medical supervision and resocialization of the patient after release from hospital. Results indicate that combination treatments with insulin and neuroleptics were most successful, and that rehospitalization is a poor indicator of treatment success because many patients are not readmitted.

003019 no author. no address **Prescribing psychotropic drugs: the primary physician's role.** Medical World News. 17(23):45-46,49,55-57,61-63,66-67, 1976.

A transcript of a panel discussion among five professionals representing general practice, internal medicine, and psychiatry is presented. Topics discussed include: 1) the main principles of giving psychotropic drugs; 2) how to determine what therapy is best for a given condition; 3) whether the initial diagnosis and treatment of minor depression or anxiety falls into the realm of the primary physician or the psychiatrist; 4) how to decide when a given drug is no longer effective and if another should be substituted; 5) how to determine the proper dosage and regimen for a specific drug; 6) problems in assessing and treating drug side-effects; 7) what measures should be taken in cases of drug abuse by the patient; 8) the significance of plasma levels in evaluating drug therapy; 9) special problems involved in treating the aged; and 10) the relationship between primary care physicians and psychiatrists.

003020 no author. no address **Cocaine "snorting" for fun.** Medical Journal of Australia (Glebe). 2(2):40, 1976.

The history and effects of ingesting and sniffing (snorting) cocaine are summarized in light of the drug's recent vogue in America. As a local anesthetic and central nervous stimulant, cocaine has legitimate medical uses, but abuse produces depression, confusion, dryness of the throat, hyperreflexia, and perhaps convulsions. Strong psychotic dependence occurs, but since there is no physical dependence, no characteristic withdrawal syndrome is experienced. It is concluded that the reemergence of cocaine as a popular drug of abuse is reason for concern. (Author abstract modified)

003021 no author. no address **Adrenergic-cholinergic imbalance in affective disorders.** Lancet (London). No. 1799:1342-1343, 1976.

The hypothesis of adrenergic/cholinergic imbalance in affective disorders is discussed. It is noted that this hypothesis has received little attention and only in the past few years have experimental studies of cholinergic factors been performed. It has been suggested that a given affective state may represent a balance between central cholinergic and adrenergic neurotransmitter activity in areas of the brain that regulate affect, with depression being a disease of cholinergic dominance and mania being the converse. It has been found that oral choline may also bring about depression in patients with normal mood, and also in patients receiving the drug as part of long-term neuroleptic treatment. Existing evidence would indicate that the adrenergic/cholinergic imbalance hypothesis should be given at least as much attention as previous biochemical theories of affective disorders.

003022 Parker, Neville. 201 Wickham Terrace, Brisbane, Queensland 4000, Australia **/Alleged psychotropic drug use in the elderly./** Comment 1. Medical Journal of Australia (Glebe). 2(2):66, 1976.

Methodological and philosophical questions regarding psychotropic drug use among the elderly are raised in response to "Psychotropic Drug Use in the Elderly: Public Ignorance or Indifference?" by Simon F. Chapman. It is argued that Chapman's data have not established a case for overprescribing in the aged; rather, they show that old people and invalids have greater need of psychotropic drugs. In addition, evidence shows that the prevalence of psychiatric disorders is increased among people over 60, so more drugs may be appropriate in this age group. It is a reasonable criticism to point out doctors' tendency to overprescribe to manage symptoms, but this tendency is not a specific issue for any age group of patients. Finally, an argument is offered for allowing the elderly the solace that drugs can offer in old age. (Author abstract modified)

003023 Pelc, I. Institut de Psychiatrie, Hopital Universitaire Brugmann, 4, place Van-Gehuchten, B-1020 Brussels, Belgium **/Sulpiride and psychic decompensation./** Le sulpiride et la decompensation psychique. Encephale (Paris). 2(4):349-361, 1976.

The use of sulpiride in states of psychic decompensation is reviewed. Following a brief statement on the therapeutic profile of sulpiride, a review is presented of its action in acute delirious states, depressive states, anxiety, autism, and in psychological stress, including several case histories. It is concluded that sulpiride has mainly three types of action: neuroleptic, anticonfusional, and antidepressant, and that states of psychic decompensation are particularly sensitive to the action of this psychotropic drug. It is suggested that its aspecific recompensation activity consists of action on the vegetative brain, as well as its antistress properties. 48 references.

003024 Rafaelsen, Ole J. Biological Psychiatry, University of Copenhagen, Denmark **Lithium: its mode and range of action.** In: Advances in the drug therapy of mental illness. Geneva, World Health Organization, 1976. 168 p. (p. 141-149).

A unifying theory of electrolyte and amine involvement for the mode of action of lithium in affective disorders and an examination of the effects of lithium treatment in manic melancholic states, Huntington's chorea, and Meniere's disease are presented. The effect of lithium on the enzyme and metabolic systems is discussed, and a review of studies and hypotheses on various affective disorders is presented. Hypotheses concerning electrolyte involvement in Meniere's disease, and amine involvement in Huntington's chorea appears to indicate an interrelationship between the pathophysiology and pharmacotherapy of these disorders in terms of inadequate transport or availablity of ions. 58 references.

003025 Reynolds, Ingrid; Magro, Dennis. Health Commission of New South Wales, 9 to 13 Young Street, Sydney, New South Wales 2000, Australia **The use of methadone as a treatment tool for opiate addicts: a two-year follow-up study.** Medical Journal of Australia (Glebe). 2(15):560-562, 1976.

To evaluate the effectiveness of methadone as a treatment for opiate addicts, 96 former participants (83% of a sample of 116 addicts treated) of a Sydney, Australia, methadone program were successfully followed up after 2 years. Methadone was not found to be a quick cure for opiate addiction; more than two thirds of the sample were still taking methadone, only 3% had not taken any opiates for 6 months or longer, and a further 5% had not taken any opiates for less than 6 months. The remainder (22%) were using illegal opiates either regularly or intermittently, or were in prison. However, from the employment, crime, and social emotional stability data, it may be concluded that the methadone program, particularly if adhered to continuously, is successful. The clients, especially those who were still adhering to the program, felt that methadone was helpful, although there was concern about still being drug dependent and about side-effects. 5 references. (Author abstract modified)

003026 Richter, Derek. West Park Hospital, Epsom, England **The pathophysiology of schizophrenia.** In: Advances in the drug therapy of mental illness. Geneva, World Health Organization, 1976. 168 p. (p. 150-157).

Selected observations on the pathophysiology of schizophrenia are presented to serve as a guide for further research. It is suggested that schizophrenia as presently defined, is not a single homogeneous condition, but a group of conditions with different causal factors leading to a final common pathway indicated by a specific set of symptoms. The underlying neurological mechanisms, genetic predispositions and symptoms associated with schizophrenia in various investigations are reviewed. Findings from studies of the pharmacological action of drugs, including mescaline, amphetamines, and phenothiazines, on the symptoms of schizophrenia, are also presented.

003027 Romeu, Joan. no address **/The neuroleptic Leponex./** "Leponex." Revista de Psiquiatria y Psicologia Medica (Barcelona). 12(8):557, 1976.

The neuroleptic Leponex presents special interest, due to the current emphasis on tolerance of pharmacologic agents even more than on efficacy. This derivative of dibenzodiazepine (clozapine) has incisive neuroleptic action, yet is notable in that extrapyramidal side-effects are minimal, and are said to be practically nonexistent at normal oral dosages of 200 to 300mg per day or as high as 600mg, and at intramuscular doses of 100 to 500mg per day. Its action is primarily on hallucinatory delirium and psychomotor agitation. Side-effects include somnolence, sialorrhea, and asthenia, and are easily controlled. Blood tests are advised to detect the appearance of erythropenia or leukopenia in susceptible patients.

003028 Rosser, Rachel. Maudsley Hospital, London SE5, England **Depression during renal dialysis and following transplantation.** Proceedings of the Royal Society of Medicine (London). 69(11):832-834, 1976.

The general management of depressive reactions in patients in end stage renal failure and in patients undergoing renal dialysis is discussed in a paper presented to the Royal Society of Medicine in England in May 1976. It is proposed that a depressive reaction is common and normal during such illness and that, while staff sensitivity and support can help patients through this period, more specialized psychiatric help is indicated if: 1) the depressive reaction is unusually severe or prolonged; 2) depression is expressed in an abnormal manner; 3) depression occurs at an inappropriate time, such as during recovery; or 4) there is no depression at all. Preventive psychiatric interventions at critical stages of the illness are recommended. It is recommended that tricyclic antidepressants should be used most cautiously if at all, because erratic variations in plasma concentrations of nortryptyline and amitryp during renal dialysis. If such drugs are considered necessary, low doses should be administered and plasma concentrations carefully monitored. 13 references.

003029 Sands, J. M.; Sands, R. Launceston General Hospital, Launceston, Tasmania 7250, Australia **Henbane chewing.** Medical Journal of Australia (Glebe). 2(2):55, 58, 1976.

An Australian case of deliberate chewing of the flowers of henbane (Hyoscyamus niger L.)to produce euphoria and the resultant poisoning is presented. The henbane plant is described and suggestions for managing henbane poisoning are given. The case was of a 20-year-old man behaving in a bizarre manner and experiencing visual hallucinations; symptoms suggested atropine poisoning. A diagnosis of henbane poisoning was eventually made when he admitted chewing the flowers. The case indicates a wider use of the weed among the drug taking community in Australia, and suggestions of diagnosis and maintenance by the physician are offered. 10 references. (Author abstract modified)

003030 Sayle, D. Norfolk and Norwich Hospital, Norwich, England **Drugs used in the treatment of mental disorder.** Nursing Mirror and Midwives Journal (London). 142(17):61-64, 1976.

A survey of the drugs used in the treatment of mental disorders is presented, based on the results of 307 examined prescription forms. The following group of drugs make up the majority of prescribed medications: 1) antidepressants; 2) tranquillizers; and 3) hypnotics. Of the total number, 63% were prescribed for females and 37% for males. Furthermore 30% were for patients 65 years of age and over, and 11% for patients 15 years of age and under. It is concluded that this survey should be repeated on a larger scale different times of the year to determine the seasonal effect on the prescription of drugs for mental disorders. 3 references.

003031 Schou, Mogens. Biological Psychiatry Psychopharmacology Research Unit, Aarhus University Institute of Psychiatry, Risskov, Denmark **Recent advances in the treatment and prevention of adverse reactions to lithium.** In: Advances in the drug therapy of mental illness. Geneva, World Health Organization, 1976. 168 p. (p. 158-168).

Adverse reactions to lithium treatment and recent advances in the treatment and prevention of adverse reactions to lithium are presented. Frequent side-effects in three categories: 1) harmless effects seen during the first days or weeks of treatment; 2) harmless effects occurring later in treatment; and 3) effects indicating impending intoxication are discussed in detail. A schedule for the treatment of a patient with lithium poisoning is proposed.

003032 Shirazawa, Hidekatsu. no address **Pharmacotherapy and confinement of patients.** Psychiatria et Neurologia Japonica (Tokyo). 78(8):576, 1976.

In a paper read at the 30th Northern Japan Psychoneurological Symposium held in September 1975 in Akita, Japan, efforts at liberalizing hospital rules and reducing the dosage of psychotropic drugs administered to patients in a Japanese hospital are detailed. Goals of the program were to gradually reduce behavioral restrictions on the patient, evaluate and promote independent activities of the patient, and increase his human contacts while reducing his medication to a minimum. Expected behavioral problems did not result from the simultaneous liberalization of the ward and the reduction of medication; in fact, there was a large reduction of untoward incidents in the ward.

003033 Silverman, Milton. no address **The drugging of the Americas.** Berkeley, University of California Press, 1976. 147 p. $8.50.

The marketing practices used by multinational drug companies in Central America and South America are criticized. The death of a depressed patient in Ecuador from a hypertensive crisis precipitated by concomitant administration of imipramine and phenelzine is cited as an example of the misuse of drugs resulting from these marketing practices. The problem in Latin America is complicated by the lack of legislation or its enforcement as well as by the availability of potent drugs by means other than a doctors' prescription. The indications, warnings, and side-effects of several drugs are listed.

003034 Silverman, P. B.; Ho, B. T. Texas Research Institute of Mental Sciences, Houston, TX 77030 **Discriminative response control by psychomotor stimulants.** Psychopharmacology Communications. 2(4):331-337, 1976.

At a symposium on the research aspects of drug induced discriminative stimuli conducted in connection with the annual meeting of the Behavioral Pharmacology Society, Durham, New Hampshire, in May 1976, recent studies on discriminative response control in nonhuman mammals were reviewed with respect to psychomotor stimulants and mechanisms of function. Several hypotheses for the mechanism of discriminative response control were evaluated. Several possible means by which stimulants might be expected to exert discriminative response control which were rejected include: 1) existence of a nonspecific drug state; 2) primary importance of peripheral effects; 3) anorexia; 4) hyperactivity; and 5) nonspecific CNS arousal. It is suggested that involvement of dopaminergic systems is the common essential feature of the ability of dopamine blocking or depleting agents' ability to control discriminated responding. 23 references.

003035 Simon, P. Departement de Pharmacologie, Faculte de Medecine Pitie-Salpetriere, 91, boulevard de l'Hopital, F-75634 Paris Cedex 13, France **/Tranquilizers: pharmacological aspects./** Les tranquillisants: aspects pharmacologiques. Encephale (Paris). 2(3):193-196, 1976.

Pharmacological aspects of minor tranquilizers were discussed at the 10es Journees d'Information Psychiatrique, Marseilles, 1976. Drugs used as minor tranquilizers include chlordiapoxide, diazepam, oxazepam, medazepam, clorazepate, lorazepam, clobazam, tofisopam, meprobamate, hydroxyzine, cyclarbamate, captodiamine, azacyclonol, mecloralurea, mesoridazine, valnoctamine, methylpentynol carbamate, trimethozine, phenpentadiol, benzoctamine, mephanoxalone, barbiturates, major tranquilizers in low doses,

alcohol, and beta-adrenergic blockers. In animals, the minor tranquilizers produce sedation, neuromuscular relaxation, and anticonvulsant activity. The minor tranquilizers also relieve experimentally induced neuroses in animals. The benzodiazepines have a large margin of safety. Their only contraindication is myasthenia. Reports of dependence are rare. The nonbenzodiazepines have a lesser margin of safety. Procalmadiol produces severe intoxication.

003036 Skoczkowski, Jacek; Krystof, Jan. Wojewodzkiej Szpital Chorob Ukladu Nerwowego, Boleslaw, Poland **/Hysterical and hysteria-like reactions during neuroleptic treatment for schizophrenia./** Reakcje histeryczne i podobne do histerii w przebiegu terapii neuroleptycznej schizofrenikow. Psychofarmakoterapia Schizofrenii Leki o Przedluzonym Dzialaniu. Wroclaw, Polskie Tow. Psychiat., 1976. 256 p. (p. 215-219).

In a paper presented at a symposuim on the Use of Long-Acting Neuroleptic Drugs in Schizophrenics held in Wroclaw, Poland, in October 1973, a study of hysterical and hysteria resembling reactions during neuroleptic treatment for schizophrenia is presented. Little previous study had been conducted in this area due to confusion of hysterical behavior with neuroleptic side-effects. However, it is proposed that hysterical or near hysterical behavior may actually be a defense mechanism specifically developed to stop the neuroleptic treatment. 24 references.

003037 Smith, Mickey C. no address **/Changes in prescribing patterns of minor tranquilizers./** no title. Final report, NIMH Grant MH-26544, May 1976.

Observed change in prescribing patterns of minor tranquilizers when changes is forced upon the prescriber by the imposition of a state Medicaid formulary were studied. Data were gathered from a stratified random sample of Mississippi pharmacies via audit of vendor claim forms for six month periods before and after the establishment of formulary restrictions, to determine the nature and suitability of drugs chosen by physicians as substitutes for minor tranquilizers no longer paid for by the Medicaid program. When the physician was faced with the closed formulary he was left with four basic choices for his patients who were receiving minor tranquilizers. He could: 1) prescribe the one remaining minor tranquilizer on the formulary; 2) switch to another nonminor tranquilizing agent; 3) continue therapy and force his patient to pay for his drugs; or 4) discontinue therapy. Results indicate that physicians chose the latter three courses of action.

003038 Solow, Robert A. University of California at Los Angeles, Los Angeles, CA 90032 **Child and adolescent psychopharmacology in the mid-seventies: progress or plateau?** Psychiatry Digest. 37(10):15-16, 19-23, 27-30, 35-38, 1976.

Some of the problems encountered by psychiatrists in treating children and adolescents, including the lack of a conclusive body of psychopharmacologic conclusions upon which the practitioner can draw for help in treating various syndromes and disorders, are discussed. Many authorities feel that there have been very few well thought out, formulated, and performed research experiments which would further the use of drugs in treating these patients. Current recommendations for usage in children and adolescents, including dosages and information about side effects, are stated for phenothiazines, butyrophenones, thioxanthenes, oxoindoles, tricyclic antidepressants, monoamine oxidase inhibitors, stimulants and anxiety drugs, based on the current literature. Individual drugs within each class are discussed. In addition, the use of lithium carbonate, megavitamins, diphenhydramine, hypnotics and anticonvulsants for children and adolescents is discussed.

003039 Somerville, Brian W. Division of Neurology, Prince Henry Hospital, Sydney, Australia **Treatment of migraine attacks with an analgesic combination (Mersyndol).** Medical Journal of Australia (Glebe). 1(23):865-866, 1976.

Treatment of acute migraine attacks with an analgesic combination was studied with special attention to the possible placebo effect in this disorder, which is strongly modified by emotional factors. Relief with an analgesic/antihistamine combination containing paracetamol, codein phosphate, doxylamine succinate and caffeine (Mersyndol) was compared with that achieved with a placebo in a double-blind crossover trial with 34 patients. Mersyndol emerged as significantly better than placebo in the complete relief of migraine pain, and was clearly superior to placebo in partially relieving the pain of migraine. These results suggest that it could be a useful alternative to ergotamine, and a comparative trial with ergotamine is suggested. Side effects with this combination were fairly common but mild, and consisted mainly of drowsiness caused by the antihistamine component. 18 references. (Author abstract modified)

003040 Tyrer, Peter. no address **The role of bodily feelings in anxiety.** Maudsley Monographs, London Institute of Psychiatry. No. 23. New York, Oxford University Press, 1976. 119 p. $18.00.

The role of bodily feelings in anxiety is reexamined, and a series of controlled studies that are instructive and should have wide clinical implications is presented. Following a historical/theoretical commentary and a review of beta-adrenergic pharmacology, the author states the aims of the studies in terms of two basic questions: 1) are beta-adrenoceptor blocking drugs suitable agents for investigating the relationship between experience and peripheral bodily changes in anxiety; and 2) are bodily feelings important in the genesis and maintenance of anxiety. Several well planned and controlled studies provide insights to these questions; some helpful methods for predicting treatment outcomes are also provided. The results of the studies are multiple, suggesting that the difference between normal and pathological anxiety is not merely one of degree. The division of anxiety into categories of psychic and somatic is a useful way to predict pharmacologic treatment response. The studies also show that effective beta-blockage may be perceived by some patients as unpleasant while for other patients it may be a preferred pharmacologic approach. Finally, the author presents a somatic/psychic continuum for morbid anxiety that reflects his hypothesis regarding the role of bodily feelings in anxiety and the place of several different types of treatment. 1 reference.

003041 van Kammen, D. P.; Bunney, W. E., Jr.; Docherty, J. P.; Jimerson, D. C.; Post, R. M.; Siris, S.; Ebert, M.; Gillin, J. C. Adult Psychiatry Branch, NIMH, 9000 Rockville Pike, Bethesda, MD 20014 **Amphetamine-induced catecholamine activation in schizophrenia and depression: behavioral and physiological effects (preliminary report). (Unpublished report).** Bethesda, MD, NIMH, 1976. 15 p.

In order to examine the behavioral and physiological effects of amphetamine induced catecholamine activation in schizophrenia and depression, 20 schizophrenic and 8 depressed patients received an intravenous infusion of 20mg of d-amphetamine and/or placebo in a double-blind study. Serial behavioral ratings, vital signs, plasma amphetamine levels, and all night electroencephalographic (EEG) sleep recordings were obtained during amphetamine and placebo administration. Following amphetamine, both schizophrenic and depressed patients showed a highly significant increase in blood pressure

and behavioral activation, as well as insomnia. Amphetamine plasma levels were similar in both groups. The schizophrenics, but not the depressed patients, showed significant increases in pulse rate and global psychosis ratings during the 30 minutes following the infusion. In contrast to previously reported findings, six of the nine schizophrenic patients in clinical remission from active psychosis demonstrated a brief but severe psychotic decompensation immediately following the amphetamine infusion, while the four schizophrenic patients receiving the highest psychosis ratings prior to the infusion showed improvement in their psychosis. The finding that those patients who were most severely psychotic improved following the amphetamine infusion is inconsistent with a simple formulation of dopaminergic hyperactivity in schizophrenia. Several hypotheses which may be relevant to the understanding of these apparently paradoxical effects are discussed. 24 references. (Author abstract modified)

003042 van Praag, H. M. Biological Psychiatry, University of Groningen, Netherlands **New developments in human psychopharmacology.** In: Advances in the drug therapy of mental illness. Geneva, World Health Organization, 1976. 168 p. (p. 127-140).

A number of developments expected to enrich psychopharmacology and to lead to a more rational use of existing psychotropic drugs are examined. Developments in antidepressants, neuroleptics, drugs used for treating addictions, pharmacological prophylaxis, hypnotics, neuroendocrinology, thyrotropin releasing hormone, anti-androgens, ACTH analogues, impulses from pharmacokinetics, psychotropic drugs, and the teaching of biological chemistry are discussed. It is concluded that if current trends continue, the psychiatrist will need to have a knowledge of biological behavior determinants. 29 references.

003043 Van Praag, Herman M.; Korf, Jakob. Department of Biological Psychiatry, Psychiatric University Clinic, Oostersingel 59, Groningen, The Netherlands **Importance of dopamine metabolism for clinical effects and side effects of neuroleptics.** American Journal of Psychiatry. 133(10):1171-1177, 1976.

The relationship between the clinical effect of neuroleptics, phenothiazines, butyrophenones, diphenylbutylpiperidines and human central dopamine metabolism was studied. The neuroleptic-induced increase in central dopamine turnover (an indicatory of the degree of dopamine receptor blocking) was found to be positively correlated with the therapeutic effect of neuroleptics and the development of hypokinetic rigid symptoms. This supplies a direct argument in support of the contention that dopamine antagonism is related to the occurrence of clinical effects. Indications were also found that neuroleptics of different chemical types do not significantly differ in their intrinsic ability to provoke hypokinetic rigid symptoms, and that the development of these symptoms depends on the patient's individual susceptibility, and that individual susceptibility is based on relatively low dopamine turnover. 28 references. (Journal abstract modified)

003044 Wetterberg, Lennart.; Backstrom, M.; Heyden, T.; Ask, A.-L.; Ross, S. Department of Psychiatry, Karolinska Institute at St. Goran's Hospital, Box 12500, S-11281 Stockholm, Sweden **Metabolic disturbances in schizophrenia: schizophrenia as an inborn error of metabolism.** In: Carlsson, C., Neuropsychiatric effects of adrenergic beta-receptor. Munich, Urban & Schwarzenburg, 1976. 120 p. (p. 78-85).

In a paper presented to a symposium on neuropsychiatric effects of adrenergic beta-receptor blocking agents held at Copenhagen, October 1975, the evidence for and against the possibility that a subgroup of schizophrenia is an inborn error of metabolism is discussed. The hypothesis that schizophrenia is caused primarily by a defective regulation of the monoamine oxidase enzyme systems is thought to be compatible with the dopamine hypothesis of van Praag and Korf and to serve as a possible model for the etiology of schizophrenia. Such a model is thought to offer a possible explanation for the therapeutic effect of propranolol which has been reported in some schizophrenic states. It is proposed that new types of drugs with a stabilizing effect on monoamine oxidase should be discovered and tested in conditions associated with an overproduction of transmitters and substances degraded by monoamine oxidase. 40 references.

003045 World Health Organization. 1211 Geneva 27, Switzerland **Advances in the drug therapy of mental illness.** Geneva, World Health Organization, 1976. 168 p. $12.00.

The neurobiological mechanisms underlying mental illness are discussed. Psychotropic drugs are examined from the point of view of screening, clinical evaluation (including ethical aspects), mode and range of action, interactions, and variability in response and the pharmacotherapy of schizophrenia and affective disorders and other psychiatric conditions is discussed in detail. A review of important advances in the field is provided. It is concluded that a common working ground has been established between clinicians and scientists of various disciplines and their collaboration has resulted in new tools for psychiatric research and the formulation of new concepts and theories of brain functions, human behaviour, and mental illness. (Author abstract modified)

003046 Zakusov, V. V. Institute of Pharmacology, Academy of Medical Sciences of the USSR, 125315 Moscow, USSR **Pharmacology of emotive behavior.** In: Airaksinen, M., CNS and behavioural pharmacology. Elmsford, New York, Pergamon Press, 1976. 344 p. v. 3. (p. 171-174).

In a paper presented at the Sixth International Congress of Pharmacology held in Helsinki, Finland in July, 1975, techniques used to study the influence of pyschotropic drugs on the emotions in animals are discussed and an attempt to compare the experimental findings obtained with various anxiolytic drugs in animals with their clinical effects in humans is reported. It should be kept in mind that most of the techniques used to study the influence of drugs on emotive behavior in animals (i.e. electrical stimulation of various areas of the brain or administration of various compounds to evoke an emotive response or studying drug effects after extirpation of different brain areas) are artificial. The exception is the technique of creating a situation that imitates the natural conditions leading to mental stress or conflict. In the comparative study, the sedative activity (evaluated by inhibition of explorative behavior), tranquilizing activity (evaluated by antagonism with corazol), the hypnotic effects (evaluated by potentiation of barbiturate induced sleep), the anticonvulsant effects, and the muscle relaxant activity (evaluated by rotarod or righting reflex tests) of diazepam, nitrazepam, oxazepam, chlordiazepoxide, meprobamate, and trioxazine were assessed in mice and their anxiolytic effects, hypnotic effects, anticonvulsive effects, and muscle relaxant effects were assessed in patients with neurosis or neurosis like symptoms. The highest correlations were found between the animal experimental data and the anxiolytic effects of the drugs in humans. Slightly lower correlations were found between the experimental data in animals and the hypnotic and anticonvulsive effects in humans and the lowest correlations were found between the ex-

perimental data in animals and the muscle relaxant effects in humans.

AUTHOR INDEX

[The 6-digit number is the abstract accession number. The next two digits are the issue number; digits after hyphen are the category number.]

H

I

J

N

O

P

T

U

V

SUBJECT INDEX

[The Subject Index is machine generated. Keywords in the titles of abstracts appear alphabetically in the left hand margin; under each keyword is a list of titles in which the keyword appears. The spelling of words in the titles of abstracts has not been changed; hence, two spellings of the same word may appear in this index -- for example, BEHAVIOR and BEHAVIOUR.]

Computer Information Services of the National Clearinghouse for Mental Health Information

Searches of the NCMHI computer-based information system will be done on request. These reader-generated bibliographies are available without charge to anyone within the mental health community.

Requests for a printout on a topic not covered by the abstracts in this issue or other NCMHI publications should be sent directly to the Clearinghouse. The request should include the inquirer's name, address, professional affiliation, and phone number, along with a clear and specific statement of the information desired. Either a letter or the order blank below should be sent to the following address:

National Clearinghouse for Mental
Health Information
Alcohol, Drug Abuse, and
Mental Health Administration
5600 Fishers Lane
Rockville, Maryland 20852

Date _____

Name of requester _____

Address _____

Organization _____

Phone number (include area code) _____

Information requested (please be as specific as possible) _____

_____

_____

_____

_____

☆U.S. GOVERNMENT PRINTING OFFICE: 1978— 274-470:6462

PSYCHOPHARMACOLOGY ABSTRACTS

Questions about Clearinghouse service should be addressed to:

Psychopharmacology Abstracts
National Clearinghouse for Mental Health Information
Alcohol, Drug Abuse, and Mental Health Administration
5600 Fishers Lane
Rockville, Maryland 20852

For information on subscriptions and the purchase of single copies of the *Abstracts* (Vol. 7 onward), please refer to page ii of this issue.

DEPARTMENT OF
HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE

ALCOHOL, DRUG ABUSE, AND
MENTAL HEALTH ADMINISTRATION
5600 FISHERS LANE
ROCKVILLE, MARYLAND 20857

OFFICIAL BUSINESS
Penalty for private use, $300

POSTAGE AND FEES PAID
U.S. DEPARTMENT OF H.E.W.
HEW 389

Fourth-Class/Book

PSA SERIA300SCIS5DUE002R 1
SERIALS PROCESSING
UNIV MICROFILMS INTL
300 N ZEEB RD
ANN ARBOR MI 48106

NOTICE OF MAILING CHANGE

☐ Check here if you wish to discontinue receiving this type of publication.

☐ Check here if your address has changed and you wish to continue receiving the type of publication. (Be sure to furnish your complete address including zip code.)

Tear off cover with address label still affixed and send to:

Alcohol, Drug Abuse, and Mental Health Administration
Printing and Publications Management Section
5600 Fishers Lane (Rm. 6-105)
Rockville, Maryland 20857

DHEW Publication No. (ADM) 78-150
Printed 1978